CERTIFICATE OF MAILING UNDER 37 C.F.R. § 1.8

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John G. Nagy, Reg. No. 30,664

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/693,577
Applicant	:	Lilip Lau, Bill Hartigan
Filed	:	October 23, 2003
Art Unit	:	3736
Examiner	:	Samuel G. Gilbert
Title		SELF-SIZING CARDIAC HARNESS FOR TREATING CONGESTIVE HEART FAILURE
Docket No.:	:	PARCR 65971
Customer No.	:	24201

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.131

Dear Sir:

I, LILIP LAU, DECLARE AS FOLLOWS:

1. I am one of the named inventors for the above-captioned patent application and I am an employee of Paracor Medical, Inc., the assignee of the present application. I am a co-founder of Paracor Medical, Inc. and I am the Chief Technical Officer.

2. I have first hand knowledge of the facts set forth herein. I declare that all statements made of my own knowledge are true and that all statements made on information and belief are believed to be true.

3. I have reviewed the Final Office action in the present application and I also have reviewed the prior art patent to Jayaraman, namely U.S. Patent No. 6,360,749 (attached hereto as Exhibit A). The Jayaraman patent issued from U.S. Serial No. 09/414,708 filed October 8, 1999. The application claims priority to Provisional Application No. 60/103,824, filed on October 9, 1998 (attached hereto as Exhibit B).

4. I have reviewed Provisional Application Serial No. 60/103,824 and found the application relates only to a biocompatible filler material injectable into a ventricle of the heart to treat symptoms of heart failure. The supporting drawings are numbered 1-4B. There is no disclosure in the provisional application of Jayaraman relating to elastic bands, which I understand forms the basis of the Examiner's rejection of the claims in the present application. The disclosure of the elastic bands first appears in U.S. Serial No. 09/414,708 filed October 8, 1999.

5. I have reviewed the claims pending in the present application and believe I have an understanding of the claim terms and of the subject matter of the claimed invention.

6. I and my co-inventor, Bill Hartigan, began working on the development of an endocardial harness at a time just before October 8, 1999, the priority date of the Jayaraman patent. All of the development work that we did was conducted in the United States at Palo Alto, California. Prior to October 8, 1999, we conceived of the subject matter set forth in the claims of the present application.

7. Attached hereto as Exhibit C are laboratory notebook pages, in my handwriting, as evidence of the development work that I did on the endocardial harness prior to October 8, 1999. The dates have been redacted, however, my signature and the signature of a witness appears on some of the notebook pages. The notebook pages are consecutively numbered and show continuous development work. On pages 47 and 48 of my lab notebook, I describe the problem to be solved relating to the treatment of

congestive heart failure. Starting on page 48, I propose a number of medical devices and methods of use to treat congestive heart failure.

8. Referring to the claims of the present application, the subject matter of claim 54 is fully supported by my lab notebook entries. At page 50 of my lab notebook (Exhibit C), I describe a reinforcement or support device that could be "spring-like and always exert a force on the ventricle that would cause its dimensions to reduce." On page 52, I disclose several embodiments of a medical device to treat the heart, including "zig-zags" or "a spring mechanism such as a coil." The coils are shown in zig-zag configuration and are non-overlapping hinge elements that are adapted to extend circumferentially around an outer surface of the heart to impart compressive force on the heart during diastole and systole. On page 57 of my lab notebook, I describe the use of "spring members" to link to nodes for treating the heart. In this embodiment, as described in my lab notebook, "the springs have a preload that causes them to contract the ventricle, the contractability and pumping efficiency might be improved. In addition, the springs might relieve load on the muscle wall by carrying tensile loading... ." The disclosed embodiments in my lab notebook can be delivered "endovascularly through a catheter." (Exhibit C, p. 58) Thus, the medical devices disclosed in my lab notebooks can be delivered minimally invasively through a catheter.

9. The dependent claims now pending in the present application are fully supported by the disclosure in my lab notebook. For example, claim 55 recites "wherein the hinge elements are adapted to extend circumferentially around the heart and are self-sizing." The coil spring depicted on page 52 of my lab notebook are adapted to extend circumferentially around the heart and are self-sizing.

10. Next referring to claim 57, the hinge elements are adapted to extend circumferentially around the heart and are "self-tensioning." Again, the coil springs are hinge elements that are "self-tensioning" and extend circumferentially around the heart.

11. Referring to claim 60 it recites in pertinent part "the hinge elements have a compliance that increases as a function of increased stretch." Again, the coil springs disclosed in my lab notebook would have a compliance that increases as the coil spring is stretched.

12. With reference to claim 61, it recites in pertinent part "the hinge elements have a compliance that does not decrease as a function of increased stretch." Again, the coil springs disclosed in my lab notebook would have a compliance that does not decrease as a function of the increased stretch of the coiled springs.

13. With reference to claim 62, it recites in pertinent part "the hinge elements are formed into strips that are adapted to extend circumferentially around the heart." The coil springs disclosed in my lab notebook at page 52 are shown as strips that are adapted to extend circumferentially around the heart. Similarly, an alternative design is described at page 58 of my lab notebook where it recites "the second design consists of a flat strip of metal from which barb extend outwardly in various directions." The flat strip of metal has barbs which extend outwardly like hinges to self-tension and self-size as they extend circumferentially around the heart.

14. Referring to claim 63, it recites in pertinent part "the hinge elements are formed into strips that are compressible to a low profile, minimally invasive delivery diameter." At page 58 of my lab notebook, I indicate that two designs would be delivered endovascularly through a catheter.

15. Referring to claim 66, it recites in pertinent part that the "hinge elements are formed from nitinol." At page 127 of my lab notebook, I disclose nitinol for use with staple material formed in a zig-zag configuration (page 131) which also can be used as a hinge element as set forth in the claims.

16. Referring to claim 68, it recites in pertinent part, "the hinge elements are compressible to a delivery diameter no greater than minimally invasive access between

the patient's ribs. At page 58 of my lab notebook, I disclose use of a catheter to deliver two different designs endovascularly, which would easily be accessible between a patient's ribs.

17. Referring to claim 69, it recites in pertinent part "the hinge elements are compressible to a delivery diameter no greater than minimally invasive access subcostally." Again, the catheter disclosed in my lab notebook can deliver the hinge elements minimally invasively through subcostal access.

18. Referring to claim 70, it recites in pertinent part "the hinge elements are compressible to a delivery diameter no greater than minimally invasive access percutaneously through the skin." Again, the catheter disclosed in my lab notebook can delivery the disclosed medical devices minimally invasively through percutaneous access through the skin.

19. After conceiving the claimed invention, I recall working diligently on an almost daily basis to reduce to practice various embodiments of the invention up until the time of filing U.S. Serial No. 60/188,282, filed March 10, 2000, for which the present application claims priority thereto.

20. Upon information and belief, I, along with my co-inventor Bill Hartigan, continued to work diligently, on a daily basis, between October 8, 1999 and March 10, 2000 when we filed U.S. Serial No. 60/188,282 relating to a cardiac harness. As evidenced by my laboratory notebook entries attached hereto as Exhibit D, I and my co-inventor worked on a daily basis toward the actual reduction to practice of a cardiac harness, culminating in the constructive reduction to practice in filing the provisional application. My laboratory notebook (Exhibit D) shows entries made on October 8, 1999; October 11, 1999; October 25, 1999; October 27, 1999; and October 29, 1999. Upon information and belief, I and my co-inventor worked in the lab on a daily basis after October 8, 1999, and periodically I would record entries in my laboratory notebook (Exhibit D) reflecting the work that was being conducted in the laboratory.

I declare under penalty of perjury under the laws of the State of California that the foregoing is true and correct and I acknowledge that any willful false statements and the like are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001 and may jeopardize the validity of the application or patent issuing thereon.

Date: Nov. 15, 2005

Lilip Lau

Express Mail No.: EM 061 018 699 US

COVER SHEET FOR PROVISIONAL APPLICATION FOR PATENT

Assistant Commissioner for Patents
PROVISIONAL PATENT APPLICATION
Washington, DC 20231

This is a request for filing a PROVISIONAL APPLICATION under 37 CFR 1.53(b)(2).

Docket Number	9347-005-888	Type a plus sign (+) inside this box →	+

INVENTOR(s) APPLICANT(s)

LAST NAME	FIRST NAME	MIDDLE INITIAL	RESIDENCE (CITY AND EITHER STATE OR FOREIGN COUNTRY)
Jarayaman	Swaminathan		Dallas, Texas
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TITLE OF THE INVENTION (280 characters max)

MODIFICATION OF PROPERTIES AND GEOMETRY OF HEART TISSUE TO INFLUENCE HEART FUNCTION

CORRESPONDENCE ADDRESS:

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ENCLOSED APPLICATION PARTS (*check all that apply*)

☒ Specification	*Number of Pages*	14	☐ Small Entity Statement	
☒ Drawing(s)	*Number of Sheets*	4	☐ Other (specify)	

METHOD OF PAYMENT (*check one*)

☐ A check or money order is enclosed to cover the Provisional filing fees.	ESTIMATED PROVISIONAL FILING FEE AMOUNT	☒ $150
☒ The Commissioner is hereby authorized to charge the required filing fee to Deposit Account Number 16-1150.		☐ $ 75

The invention was made by an agency of the United States Government or under a contract with an agency of the United States Government.

☒ No. ☐ Yes, the name of the U.S. Government agency and the Government contract number are: _____

Respectfully submitted,

Alan A. Fanucci (39,673) for

Signature Allan A. Fanucci
Allan A. Fanucci
PENNIE & EDMONDS LLP

REGISTRATION NO. (*if appropriate*) 30,256

Date October 9, 1998

☐ Additional inventors are being named on separately numbered sheets attached hereto. Total number of cover sheet pages. 1

PROVISIONAL APPLICATION FILING ONLY

MODIFICATION OF PROPERTIES AND GEOMETRY OF HEART TISSUE TO INFLUENCE HEART FUNCTION

FIELD OF THE INVENTION

This invention relates to treatment of heart failure and more particularly, treatment of heart failure by reducing the internal volume of a dilated and diseased left ventricle.

BACKGROUND OF THE INVENTION

Disabling pump failure of the heart due to both ischemic heart disease (myocardial infarction) and non-ischemic cardiomyopathy is a common occurrence. This condition is frequently refractory to medical treatment, leaving heart transplantation as a last resort for some individuals. For many patients there are no viable options, either to treat the condition or even to bridge the time until heart transplantation can be performed.

Surgical modes of intervention for the treatment of heart failure include: stiffening zones of acute infarction, for example by directly injecting glutaraldehyde into the affected tissue; wrapping a skeletal muscle (stimulated electrically) around the heart to augment ventricular contractility; and applying an epicardial marlex mesh to support the weakened and distended left ventricle.

Alterative treatments include implantation of an artificial heart, an example of which is the diaphragm pump described in U.S. Patent 4,468,177. The pump disclosed in this patent comprises two chambers which are driven in a "push-pull" manner so that the volumes of each of the two chambers are alternatively enlarged and reduced and, further, both chambers are in the path of fluid through the pump. However the use of this pump arrangement for total heart replacement or heart assistance would require an extremely reliable, durable and portable power supply. Although mechanical pumps have been constructed and tested, they have not been found to be adequate for the treatment of heart failure.

A decrease in the internal volume of the damaged left ventricle will increase its efficiency because the amount of oxygen consumed by the myocardial muscle as it pumps is related to the wall tension developed during ventricular contraction. The wall tension, in turn, is proportional to the fourth power of the diameter of the ventricular cavity. Therefore, at a given smaller diameter, less work will be used by the muscle to pump a given volume of blood against a given pressure.

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Cardiac output has been improved surgically by reducing the volume of a diseased left ventricle. Removal of the non-functioning aneurysmatic segment of the heart muscle has improved the hemodynamic situation by changing the geometry of the left ventricle, leading to enhanced cardiac output. However, this procedure, generally referred to as the Batista technique, is associated with considerable operative risk.

An improvement upon this operation is disclosed in U.S. Patent 5,738,626. In this modified surgical procedure, which includes elements of the other approaches as well, the dilated left ventricle is first reduced in size via myocardial resection and then the heart is supported and assisted by the attachment of a cardiomyoplasty muscle wrap. A disadvantage of this, or in fact any, cardiomyoplasty procedure is that the tissue used for the ventricular wrap is skeletal muscle which fatigues upon repeated stimulation at normal heart rates. Therefore, a period of time exceeding several weeks is required after this operation to condition the skeletal muscle, transforming it into a different tissue, rich in mitochondria and adapted to withstand the repeated stimulation with much less fatigue. During this period a ventricular assist pump may be implanted within a hole cut in the ventricle. Eventually, this assist pump will be removed.

Therefore, there is a need for a less aggressive method for volume reduction of the left ventricle in order to treat heart pump failure. This invention provides an alternative approach for the treatment of heart failure that is less invasive than surgical procedures currently available.

SUMMARY OF THE INVENTION

This invention is directed toward treatment of heart failure by physically modifying the diseased or damaged heart tissue in such a manner that the internal volume of the damaged left ventricle is reduced, thereby improving the pumping efficiency of the diseased heart and ameliorating the symptoms of heart failure.

One embodiment of this invention comprises a catheter-based, minimally invasive procedure that will introduce biocompatible materials into the left ventricle of the heart. Part of the left ventricular cavity will be filled with biocompatible material which will be applied and attached to the left ventricle using catheter-guided techniques and equipment rather than conventional cardiosurgical procedures. The biocompatible filling materials introduced will decrease the volume of the left ventricle and improve the hemodynamics of the heart, thereby alleviating the symptoms of heart failure.

A second embodiment, which may be used either alone or in combination with the first embodiment, comprises direct injection of suitable, substantially non-compressible biocompatible materials into the wall of the left ventricle. This procedure

will increase the bulk of the wall and thereby diminish the interior volume of the left ventricle. These materials may also strengthen and reinforce the wall as well, diminishing the risk that the ventricle might rupture.

The biocompatible filler materials to be used in both embodiments of this invention will exist in a substantially liquid state while they are delivered to the heart. They will then be converted to a second, substantially rigid state when they are attached to or injected within the wall of the left ventricle. Also contemplated in this invention are filler materials which will expand to a pre-determined volume as they undergo the transition from the first, substantially liquid state to the second, substantially rigid state. These could also be foam-like materials which increase or decrease in size depending on the desired mechanism of action.

BRIEF EXPLANATION OF THE DRAWINGS

Figure 1 is a schematic representation of a diseased left ventricle of a heart depicting the left ventricular aneurysm (2) present in the diseased portion of the left ventricle. This figure also displays peripheral vascular access to the damaged site (3) and the non-diseased section of the left ventricle (1).

Figure 2 depicts the catheter to be used for the application of filling materials into the left ventricular cavity, the filling material expanding after release from the catheter, the screw-like fixture holding the catheter in place and the expanded stabilizing skeleton.

Figure 3 reveals the release mechanism and the presence of the filling material in the left ventricle as the application catheter is withdrawn.

Figure 4 represents the filling material within the stabilizing structure attached to the wall of the left ventricle after removal of the application catheter (4 A). This figure also depicts (4 B) filling material which could be contracted while still attached to the wall of the left ventricle, thereby decreasing the internal volume of the left ventricle.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

This invention describes approaches to be taken for the treatment of heart failure which avoid resection of diseased heart muscle. In one embodiment of this invention, part of the diseased, expanded left ventricle will be partially filled with biocompatible materials which either will be attached to the wall directly or to a stabilizing skeleton attached to the wall. This will modify the geometry of the heart due to the introduction of the biocompatible material to decrease the internal volume of the left ventricle and thereby improve its geometry and hemodynamics. In a second embodiment, which may be used

independently or in conjunction with the first embodiment, appropriate, biocompatible materials may be injected directly into the diseased tissue thereby thickening, reinforcing and strengthening or revitalizing the cardiac wall and, simultaneously, decreasing the internal volume of the left ventricle, thereby increasing cardiac efficiency.

Damaged regions of the left ventricular cardiac wall may be defined and mapped by procedures well known in the art including both computer imaging and ventricular wall motion analyzers. Once this has been done, either or both embodiments of this invention may be utilized to treat heart failure resulting from the damage to the wall of the left ventricle.

The first embodiment of this invention comprises the use of a catheter for the introduction of biocompatible materials into the left ventricle. These materials may be coated upon or within a supporting skeleton within the heart. This embodiment also encompasses the delivery of filler materials into a container that may either be attached directly to the cardiac wall within the left ventricle or it may be attached to a stabilizing skeleton that will be fixed to the wall of the ventricle.

This embodiment also encompasses application of suitable biocompatible materials directly to the surface of the wall of the left ventricle. These filler materials may be used to increase the bulk of that part of the cardiac wall, decreasing the volume of the left ventricle. These materials may also be used to induce the retraction of the wall to which they are attached. Here the filler materials on the wall would shrink, condense or retract as a result of a physical or chemical change, causing a corresponding retraction of the wall of the ventricle. In addition, the state of phase of the material can be converted as it is introduced into the heart to cause expansion of the material and reduction of the volume of the heart.

Another embodiment of this invention comprises direct injection of biocompatible materials into the diseased tissue of the left ventricle to revitalize it or to increase its bulk and, consequently, improve the properties of the wall and to decrease the internal volume of the left ventricle. Suitable materials for this purpose would include, but not be limited to, angiogenic agents, collagen, fibrinogen, foams or hydrogels which are well known in the art. More generally, this invention contemplates the use of the group of substances referred to in the art as "polymeric endoluminal paving system" materials as biocompatible filler materials. Heart failure could be treated with such injections, either alone or in conjunction with the decrease in the volume of the left ventricle that would be obtained through the first embodiment of this invention.

The embodiments of this invention will employ a steerable application catheter which will be introduced into the left ventricle either by direct percutaneous access or by transluminal vascular access by retrograde passage of the aortic valve. The application catheter will be capable of being reversibly attached to the cardiac wall. Attachment of the

steerable application catheter to the wall of the ventricle will allow the precise and accurate delivery of biocompatible filler materials, stabilizing skeletons, cutting means and tissue removal means to predetermined locations within the heart.

Furthermore, the application catheter will transport a stabilizing skeleton attached to the catheter by a reversible release mechanism. The application catheter may carry the stabilizing skeleton either internally or externally. The release mechanism, deploying the stabilizing skeleton, will be reversible to allow the retrieval of the stabilizing skeleton.

The application catheter may also be attached by a first reversible attachment means to a stabilizing skeleton which, in turn has a second reversible attachment means by which it may be attached to the wall of the ventricle. In this illustration of the invention, the catheter is attached only indirectly to the wall of the ventricle through the stabilizing skeleton. Furthermore, in this instance, the delivery means for the biocompatible filler material would be located at a point on the stabilizing skeleton proximal to the second attachment means and distal to the junction between the catheter and the stabilizing skeleton defined by the first attachment means.

The application catheter will further comprise an anchoring, screw or screw-like means for fixing the stabilizing skeleton to the wall of the left ventricle at one or more points. The stabilizing skeleton may comprise arrangements of flexible filaments or elastic wires comprising suitable, biocompatible materials. The stabilizing skeleton may also comprise a network or mesh of such filaments, and in addition, a flexible, expandable container.

The application catheter of this invention will also have cutting and retrieval elements. These will allow removal of part of the cardiac wall as needed, for example, for attachment of the application catheter, attachment of the stabilizing skeleton, application of suitable materials to the surface of the cardiac muscle, and injection of the filler material into the wall. The cutting and retrieval elements of the application catheter may also be used to remove the filler material from the heart, prior to the extraction of the support skeleton if that were to become desirable or necessary.

The application catheter of this invention will also comprise means by which the biocompatible filler material will be coated upon or inserted within the wall of the ventricle. The catheter will include elements for directly applying the substantially liquid filler material to the surface of the ventricular wall. It may also carry suitable means to initiate the physical and chemical changes that may be necessary to allow the biocompatible filler material to adhere to the surface of the wall. The application catheter will include components for the injection of biocompatible filler material into the wall. These components include needle-like elements for injection of materials, where the needle or

needles are positioned substantially perpendicular to the site of injection. The injection component may also be composed of a number of needle-like elements placed at the proximal end of the catheter. These needle-like elements could be attached to the catheter at an angle of approximately 30° to the longitudinal axis of the catheter to allow a wider area of the wall of the ventricle to be treated at one time. Also contemplated are needle-like means projecting radially from the application catheter. Here the catheter may be placed within the heart wall, using for example a void or pit constructed with the cutting and retrieval elements described above. The filler material would then be injected in a direction substantially perpendicular to the long axis of the catheter and substantially parallel to the surface of the cardiac wall. This embodiment of the invention contemplates multiple, retractable needles allowing a radial dispersion of the biocompatible filler material within the cardiac muscle.

The biocompatible filler materials will be in a fluid, substantially liquid state before they are introduced into the ventricle. Once in place these materials may undergo a phase transition into a substantially non-compressible form, essentially rigid state, as they are attached to or injected within the wall of the ventricle. The biocompatible filler may also be a material that may be both compressible and expandable. In this instance, the filler material would first be compressed while it is delivered to the heart and then allowed to expand to a pre-determined volume within the heart. The filler material will be extruded from the application catheter onto the supporting skeleton which may further comprise a flexible, expandable container. The filler will be firmly attached to or confined within the supporting skeleton in order to avoid embolization caused by the flow of the blood stream and the dynamics of the heart.

The expandable, flexible container contemplated by this invention may be attached directly to the cardiac wall or to a stabilizing skeleton that is fixed to the wall. In this approach, the filler material or materials will be injected into the skeleton or a container, expanding it to a pre-determined final volume. Once filled, the container will then be sealed. Materials which can be used to fill the container would include not only the biocompatible materials applied directly to or injected within the wall of the ventricle but they could also include, for example, colloidal suspensions, contrast mixtures and saline solutions.

Expansion of the biocompatible filler may be driven by a number of mechanisms. The filler material may expand upon release as a result of its inherent mechanical properties, as represented by a foam or as a nitinol based substance. The expansion could also be the result of an interaction between the filler material and blood or between the filler material and the tissue surface. The expansion may also be the result of the temperature and/or pressure differences between those within the heart compared to the comparable conditions found in the delivery apparatus.

The filler can also be a foam material that increases its volume upon deployment. Typical foam materials include polyurethane foams such as IVALON™ or hydrogel plugs as these materials are well known biocompatible fillers that are used in other medical applications.

This invention also contemplates the expansion or phase transition of filler material by the injection of liquids into a fluid-tight, sealable compartment containing the filler material. Suitable liquids, again, include colloids, saline solutions, contrast mixtures, or mixtures thereof.

These compartments might also allow the generation of a substantially non-compressible substantially rigid filler material through a chemical reaction *in situ*. Reagents and catalysts, if appropriate, could be provided through independent lumina of a multi-channel catheter. The reagents would be mixed and allowed to react within a sealable, fluid tight, flexible container held within the stabilizing skeleton attached to the wall of the left ventricle. The product of this reaction would have a pre-determined volume and a shape that could be constrained by a container, a stabilizing skeleton, or an expandable container held within the stabilizing skeleton. For example, reversible hydrogels may be constituted using self-assembling artificial proteins. Such protein solutions, adjusted to a first pH level could be used to fill and expand a fluid-tight container held by the support skeleton within the diseased left ventricle. Subsequent adjustment to a second pH would then induce a reversible transition of the protein solution to a substantially non-compressible, substantially rigid gel. Suitable hydrogels, with properties that would present specific advantages for application in this invention could be designed and produced by recombinant DNA methods known in the art. (Petka et al., "Reversible Hydrogels form Self-Assembling Artificial Proteins, (1998) *Science* 281 (17 July 1998), 389 - 392).

This invention further contemplates biocompatible filler materials which could be expanded to a pre-determined volume by the application of an external influence. Examples would include the expansion of suitable biocompatible fillers mediated by exposure to ultraviolet, ionizing or other radiation of an appropriate wavelength.

Still further, this invention contemplates direct attachment of the biocompatible filler material to the wall of the left ventricle. Contraction, shrinkage or compaction of a layer of filler material directly attached to the wall of the ventricle would result in a parallel contraction of that wall, thereby decreasing the internal volume of the left ventricle. Contraction of the filler material directly attached to the wall could occur over a period of time as a consequence of the nature of that material within the cardiac environment. Contraction might also occur only after a certain time period and could be mediated by the application of external factors. Such factors might include exposure to radiation of a suitable wavelength and intensity, electricity or other physical influences,

injection of other interacting materials, application of a localized source of heat or suction applied to the biocompatible filler attached to the wall of the left ventricle.

The stabilizing skeleton may be made up of biocompatible, flexible mesh-like materials, flexible filaments or from an arrangement of elastic wires. The stabilizing skeleton will include means for reversible attachment to both the application catheter and the cardiac wall. It will also be capable of collapsing into a compact structure that may transported, either upon or within the attachment catheter, to, or from, the site of its attachment within the body. Once set in place within the body the stabilizing skeleton will be expanded to the shape and size with which it will be used for the attachment of filler materials. The stabilizing skeleton may also contain within it, or have attached to it, an expandable container into which filler material can be injected.

The stabilizing skeleton may also be used for the mechanical support of a pre-determined section of the wall of the left ventricle. This structure could be applied to the internal surface of the left ventricle prior to the injection of biocompatible filler materials within the wall.

In another embodiment, the biocompatible filler is added by injection through the disease heart wall. A variety of suitable syringes are useful for this purpose, with the biocompatible material carried by the syringe body and then injected through the needle into the heart. One of ordinary skill in the art can select an appropriately sized needle to deliver the selected biocompatible material *via* this pericardial access.

In addition, the biocompatible material can be, or include, a genetic material that operates on the heart tissue over time to enhance its mass or performance. Typical genetic materials include angiogenic factor or growth factor, and these are preferably added with a biocompatible material so that the biocompatible material initially reduces the volume of the heart followed by the action of the genetic material on the heart wall over time.

The amount of biocompatible material filler to be introduced is that which will reduce heart volume to levels that control the diastolic ("D") and systolic ("S") levels to desired ranges. Typically, the heart ejection function ("F") can be calculated by the following equation:

$$F = [\ (D - S)/D\ ] \times 100\%$$

Values of 60 to 75% and particularly 65% are desired. Thus the optimum volume of biocompatible material to be introduced into the heart is that which can increase the F value to 65%. Example 1 illustrates how this is done.

The methods and means by which this invention leads to a reduction in heart volume may be understood more clearly by reference to Figures 1 to 4. As represented in Figure 1, heart failure may be the result of an aneurism (2) that has formed in the wall of the left ventricle (1) of the heart. The expanded ventricle functions inefficiently not only because

of the presence of damaged, poorly functioning cardiac tissue unable to pump effectively, but also because of the increase in the volume of the left ventricle resulting from dilatation of the cardiac wall within the aneurism. The ensuing cardiomyopathy is life-threatening and a successful medical intervention necessitates an improvement in the ability of the heart to contract effectively . Non-surgical access to the damaged regions, both for diagnosis and treatment, may be obtained through the peripheral vascular system (3).

In one embodiment of this invention, depicted in Figure 2, a catheter (4) is passed through the peripheral vascular system into the left ventricle (1). Once in position, the catheter is attached to the cardiac wall using a screw-type reversible attachment member (6). A suitable biocompatible filler material (5) is then extruded through the catheter and into the left ventricle where it will expand, solidify and adhere to a stabilizing skeleton (7) which would have been previously deployed within the left ventricle, and may, in fact, be attached to the cardiac wall through reversible attachment means.

Figure 3 depicts the solidified filler material (5), attached to the stabilizing skeleton (7). This figure also reveals another reversible attachment means (8) for connecting the catheter (4) with the stabilizing skeleton (7). Once the filler material, attached to the stabilizing skeleton, is in place, the catheter (4) is detached from the stabilizing skeleton (7), by means of the reversible connection (8) between the catheter and the stabilizing skeleton, and withdrawn from the heart.

Figure 4A depicts the removal of the catheter (4) from the heart, with the biocompatible filler material attached to the stabilizing skeleton (9).The expanded filler material (10), in place within the left ventricle, will thereby decrease the internal volume of the heart and improve the pumping efficiency of the left ventricle. Figure 4B depicts an embodiment in which the biocompatible filler material has contracted after it had been put in place, drawing the attached cardiac wall, thereby further decreasing the internal volume of the heart.

EXAMPLE

An angiogram is used to determine the heart rate of a subject, and found that D = 180, S = 100, and F is 44.4%. Computer modeling of the heart is used to image the heart and determine where dead or non-functioning tissue is located.

A biocompatible filler material of a hydrogel is placed in the heart in the area of the non-functioning tissue. After the material is placed, another angiogram is taken to find that D = 170, S = 100 and F is 42%. The preceding steps are repeated until F is increased into the range of 60 to 75% and preferably, as close to 65% as possible. The final values of D = 150, S = 90 and F = 60% are acceptable and the procedure is terminated.

THE CLAIMS

What is claimed is:

1. A method for treating heart failure comprising:
delivering into the left ventricle at least one filler material in a substantially liquid first state; and
converting the at least one filler material within the left ventricle to a second substantially non-compressible, substantially rigid state affixed to the left ventricle;
whereby the internal volume of the left ventricle is decreased.

2. The method of claim 1 further comprising applying the filler material in a substantially liquid first state onto the surface of the wall of the left ventricle, and converting the biocompatible filler material to the rigid second state to attach the biocompatible filler material to the surface of the wall of the left ventricle.

3. The method of claim 1 further comprising injecting the at least one filler material into a wall of the left ventricle before converting the filler material to the rigid state.

4. The method of claim 1 further comprising introducing a steerable catheter into the left ventricle and attaching the catheter to the wall of the left ventricle by a reversible attachment means, for delivery of the filler material.

5. The method of claim 4 further comprising:
introducing a catheter reversibly attached by a first attachment means to a collapsed, flexible, expandable, sealable container into the left ventricle, the catheter further comprising a sealing means;
attaching the catheter to the wall of the left ventricle by a second, reversible, attachment means;
attaching the container to the wall of the ventricle by a third, reversible, attachment means;
delivering the filler material through the catheter into the container within the left ventricle ;
converting the filler material in the container within the left ventricle to the second state;
sealing the container;
detaching the catheter from the container by the first attachment means;
detaching the catheter from the wall of the ventricle by the second attachment means; and
withdrawing the catheter from the left ventricle.

Fig. 1

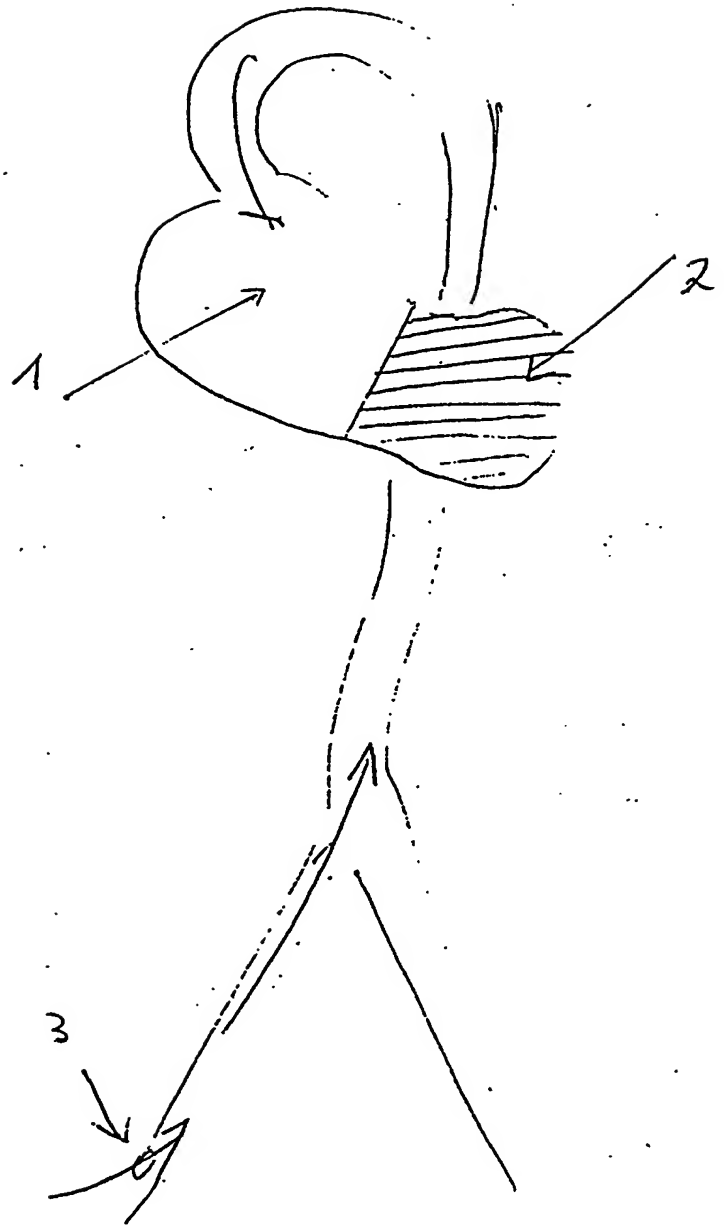


Fig (4) A

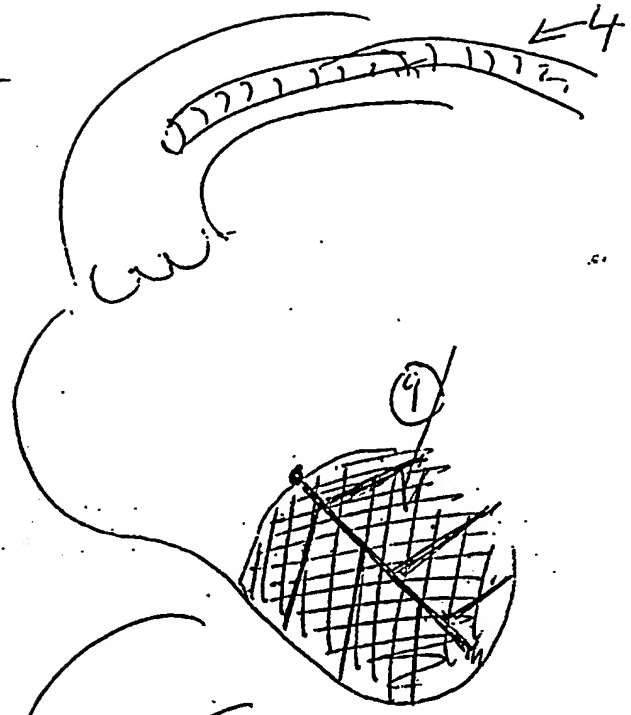
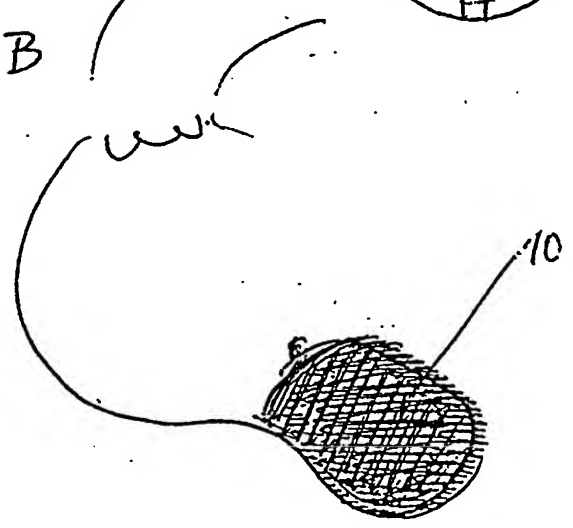


Fig (4) B



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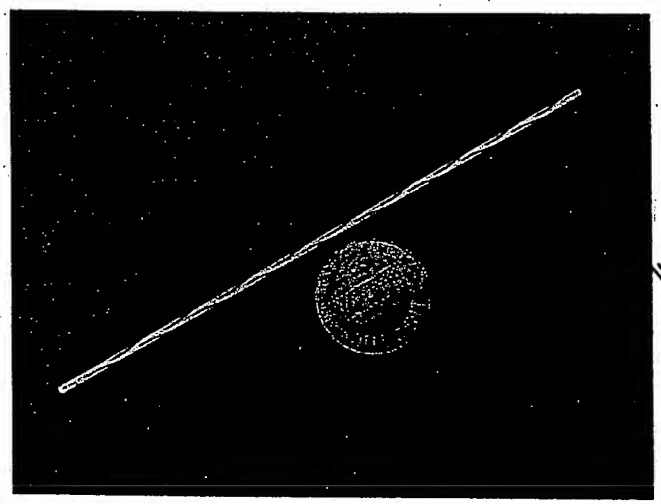
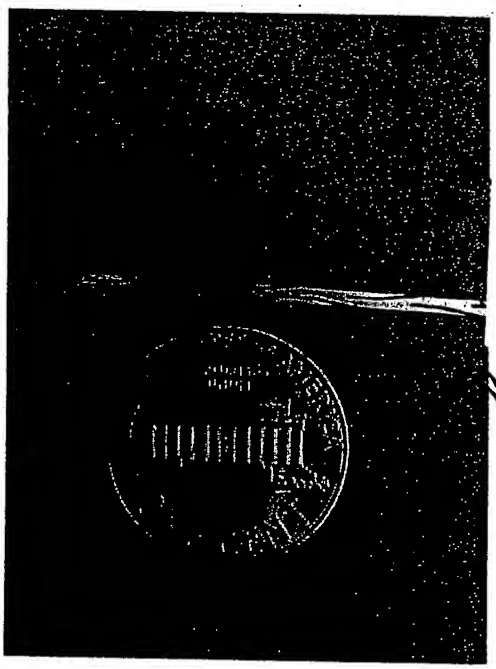
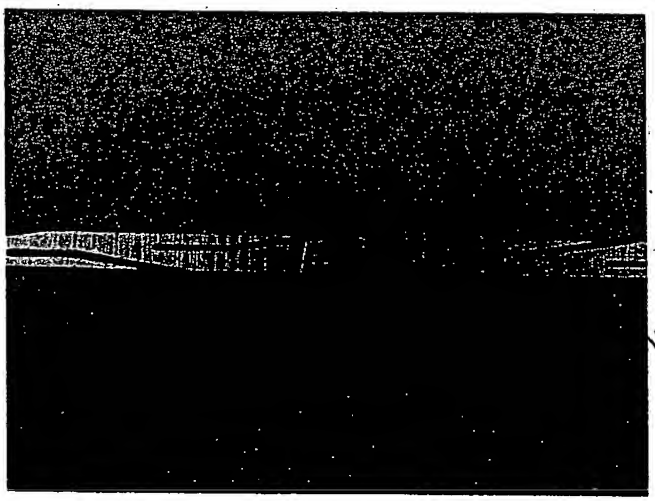
Evaluation of AN-11A Staple Prototypes

Photoetched stainless steel prototypes were received of the "AN-11A" staple design were received and evaluated.







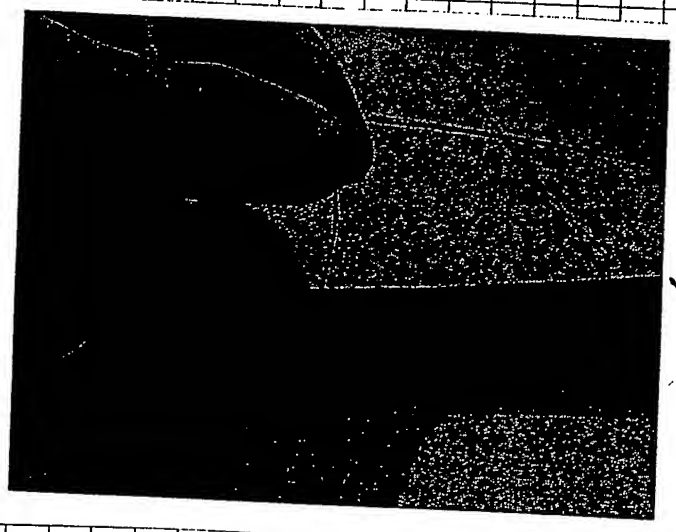
In the flat configuration shown the barbs are flush with the surface and accordingly, the surface is smooth. When the staple is bent, by applying a moment to the ends, the barbs

can be seen to project away from the surface. The extent of projection appears to be proportional to the bending moment distribution along the staple.

At the ends, the barbs are flush whereas in the middle the barbs appear to project the greatest amount.

The staple was manually applied to a piece of butyle rubber bicycle inner tubing ~~by hand~~. The staple was held at approximately perpendicular to the surface of the rubber. The staple was then applied

to the surface by pressing down on it in a direction perpendicular to it. At some point near the surface the staple buckles so that the barbs just above the buckle point project down away from the staple and down toward the surface. As down ward force continues to be applied the barb is driven perpendicularly into the surface of the rubber, much like driving a sewing needle into a substrate.



barb in photograph seen to be directed at tissue surface

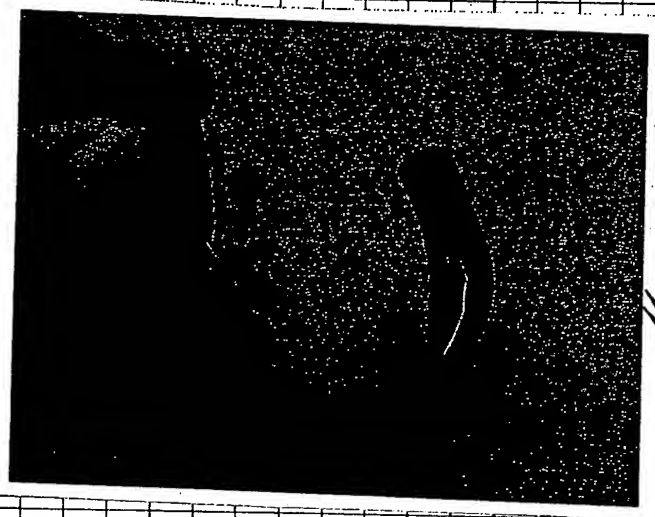
As more force is applied to the staple it causes the buckle point

to move up along its length. Thus causes the staple to advance along the surface of the rubber substrate. As it advances, the barbs that have already been driven into the tissue flatten out against the surface of the tissue, essentially closing their previous projection. Because the stainless steel staple material is somewhat malleable the buckling imparts a residual deformation or curvature to the staple. Thus when applied to a flate surface the staple ends up being somewhat curled. If the staple were made of a "superelastic" material such as nitinol, the material might recover and resist the curling phenomenon.

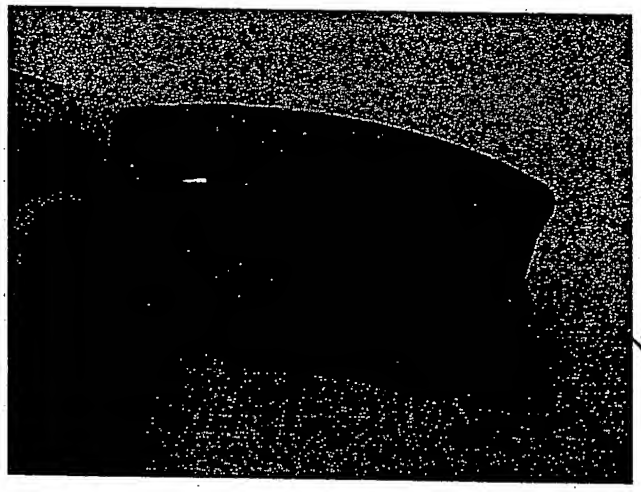
It was also noted that the barbs were very sharp and stiff and were driven

into the rubber easily.

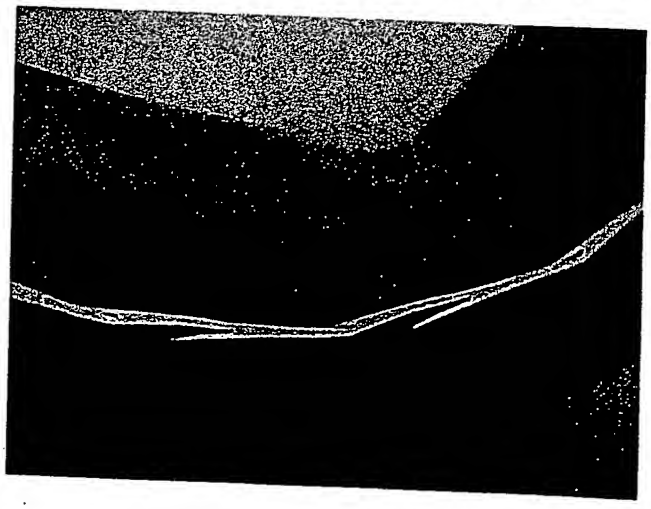
← Top View



Side View. shows curvature →



← Back side shows barbs after penetrating 2 layers of rubber.



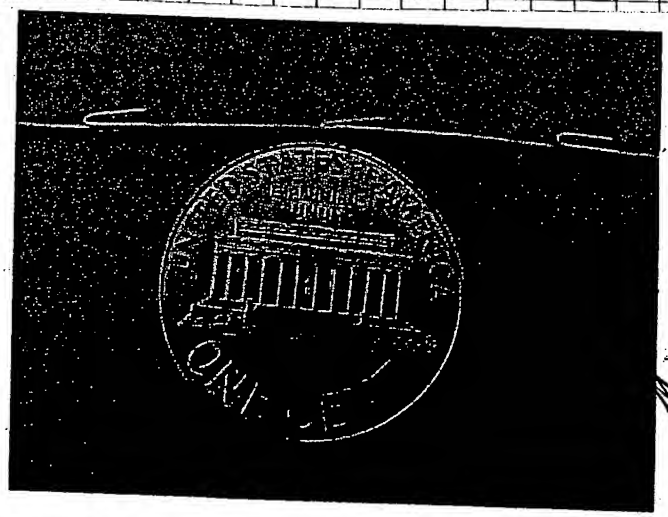
Close up of → barbs + staple.

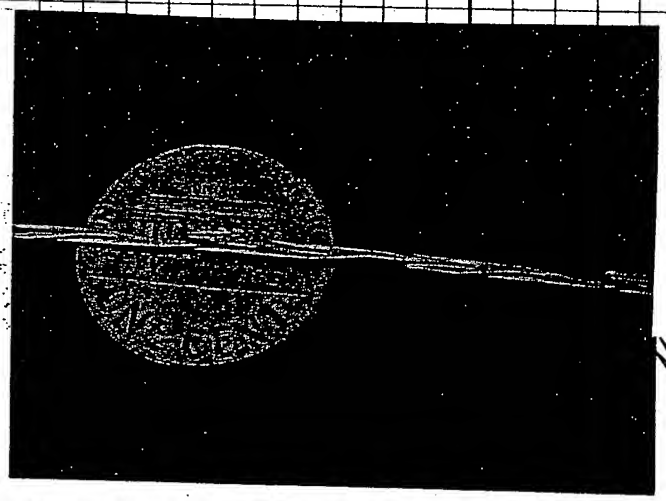
An additional evaluation was performed by manually applying the staple circumferentially around the inner wall of a Surgitek rubber tube. The staple and barbs were also seen to apply easily. In addition they appeared to attach firmly and securely to the substrate.

Axially (along the lumen) oriented force was applied to the staple. The staple appeared very resistant to this. Circumferential force in a direction opposite that of the barbs, however, caused the staple to separate from

the rubber surface readily. To remedy this several modifications were contemplated.

← Sideways flaring of staple barbs.





Reversed (180°) orientation of several barbs.

Pamela Kan

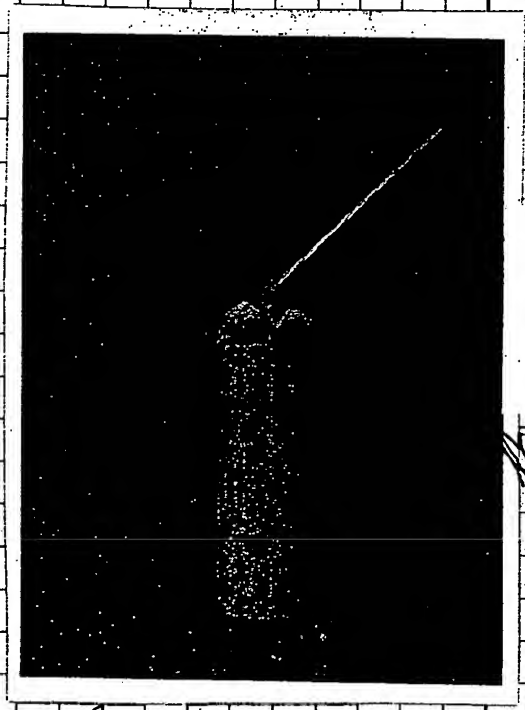
Philip Kan

Circumferential Stapling Simulation

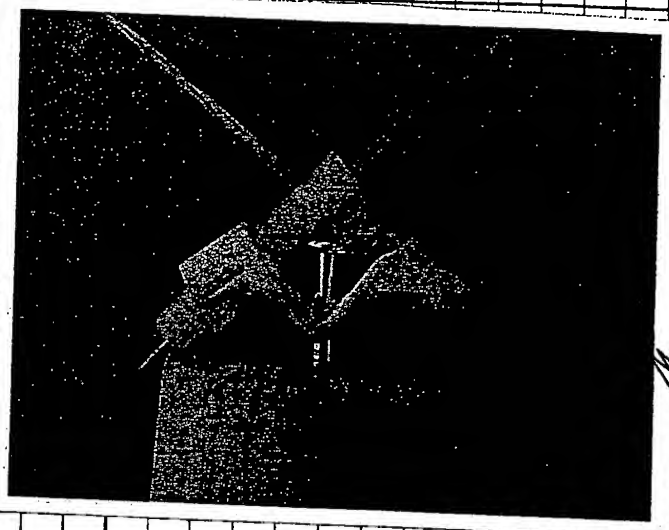
A fixture was constructed to simulate the endovascular / endoluminal delivery of the AN-11A staples circumferentially against a vessel wall through a catheter.

The set up consisted of a wooden dowel base with two plastic tubes pivotably fixed to its end. Staples would be pushed out of the tubes against a butyl rubber inner tube lumen wall.

Dowel with pivotable plastic fixture holding 2 plastic staple tubes at roughly 90° angle to each other.

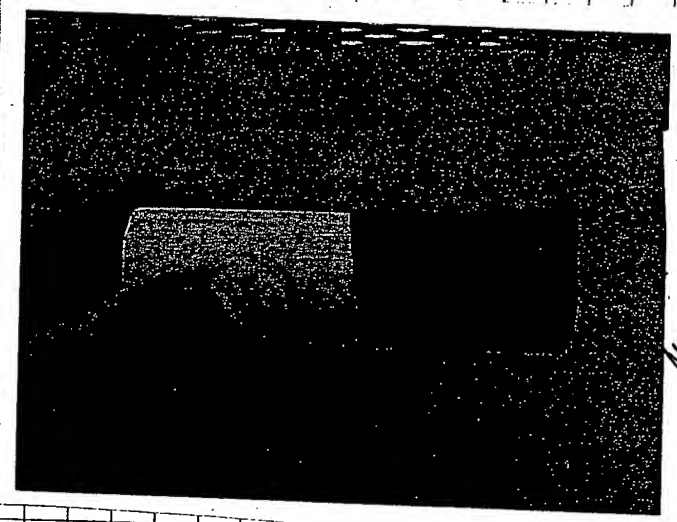


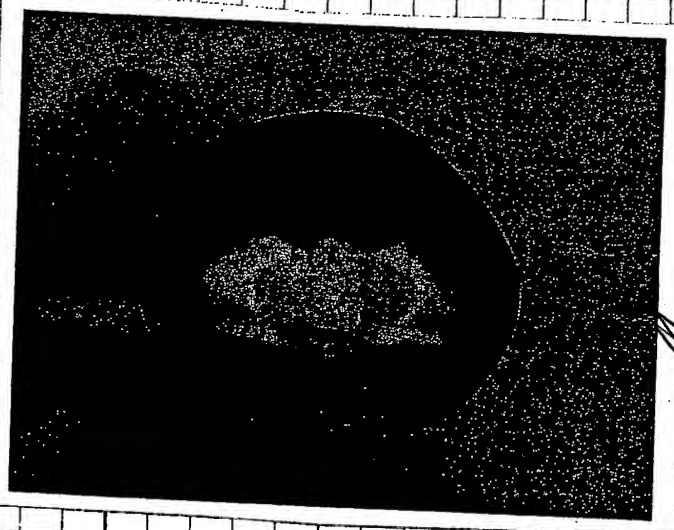
2 staples (AN-11A) inserted into plastic tubes



← Close up of staples in plastic tubes.

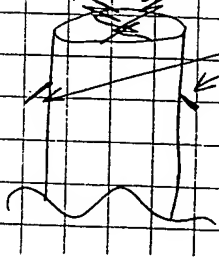
Butyl rubber inner tube pulled over plastic tube fixture and dowel. →

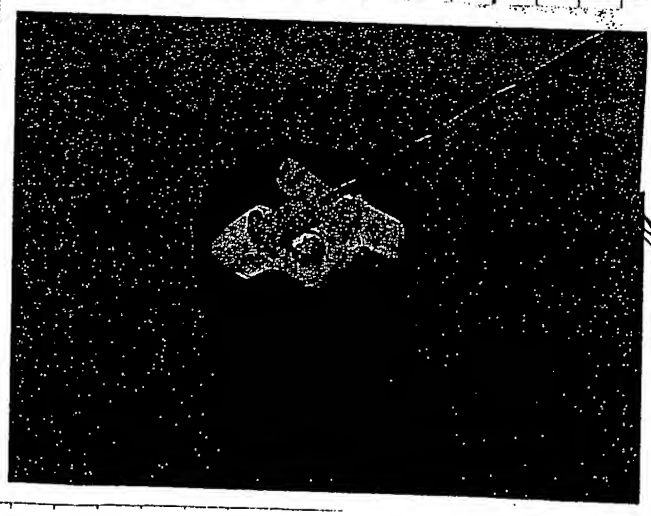


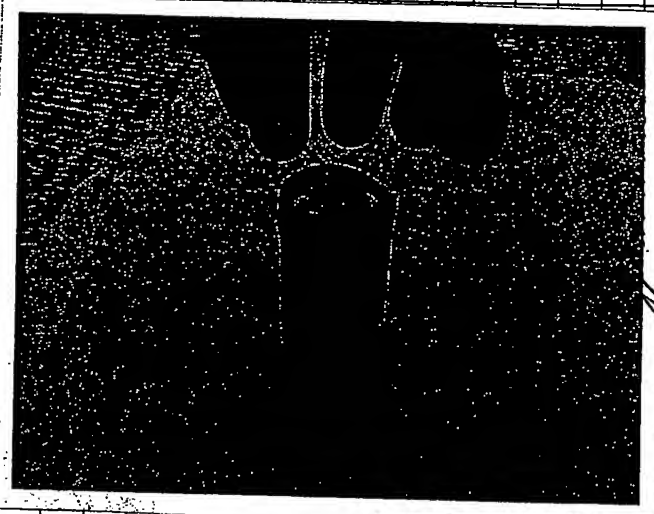


← End view of above ↑
Plastic tube openings are positioned adjacent to rubber tubing wall

Staple reinserted into plastic tubes and driven into rubber tubing →

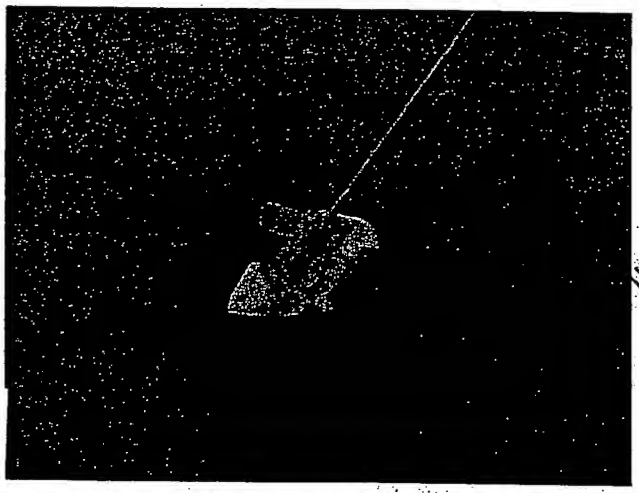




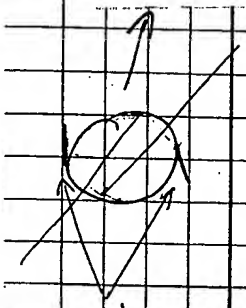


— Manual, even pressure applied on the 2 staples only

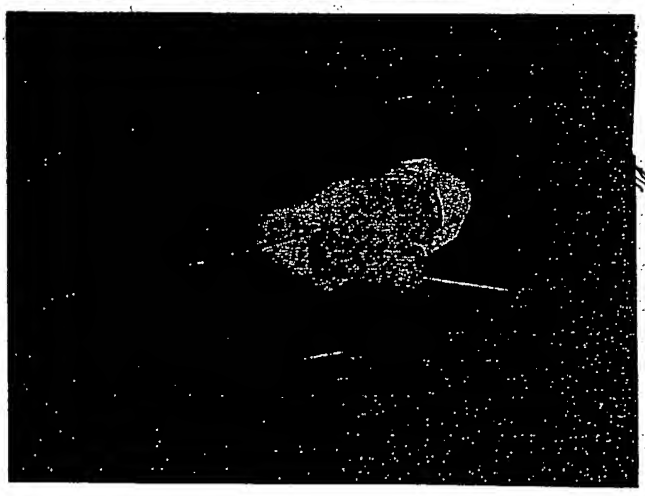
staples have buckled, causing the tube holding fixture to rotate ccw about central axis — staples begining to attach to wall.

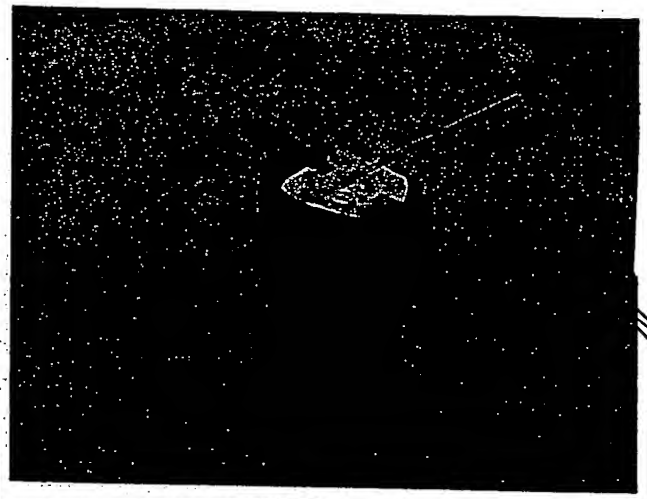


← rotating of fixture & attachment of staples continues as force continues to be applied on staples - First barbs are turned away from direction of fixture travel



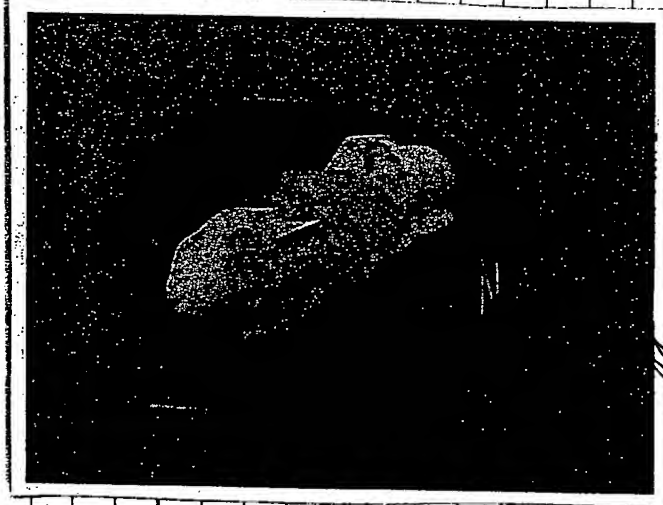
Approximately 60° 120° of wall attached to each staple



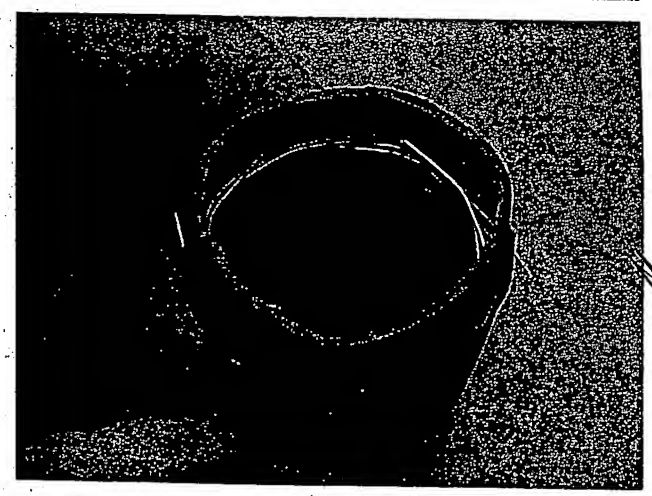


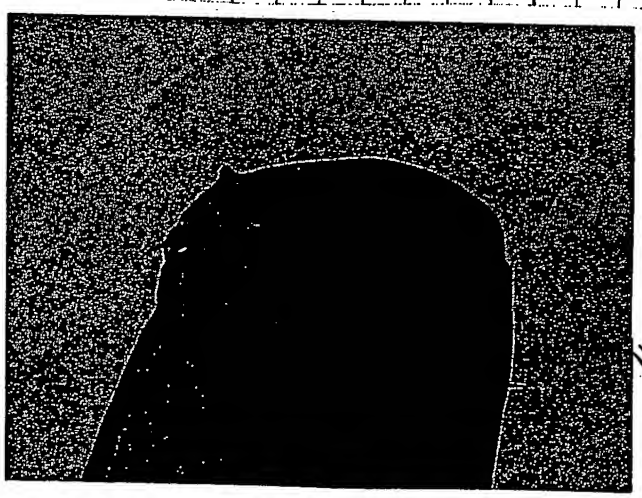
← continuation - outward bulge of tubing seen at staple line.

continuation



← stapling complete





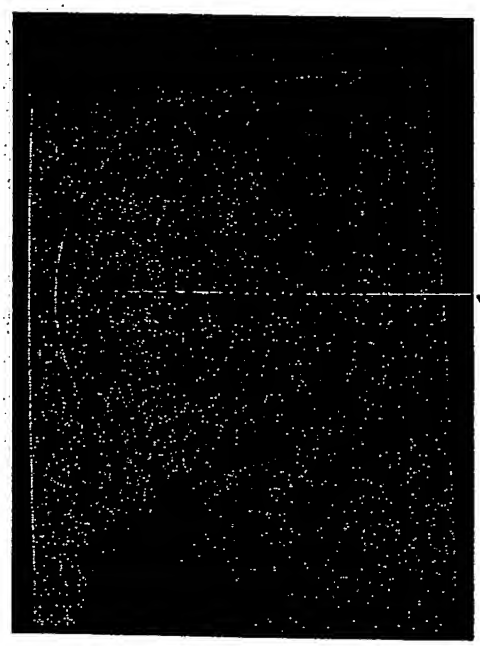
← after tubing removed - overlapping staples visible - also - staples are flush against wall and needles are seen protruding from outer surface of tubing →

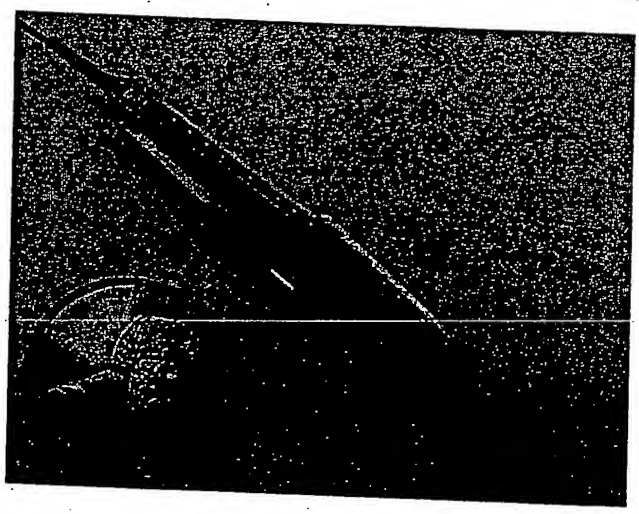
The application of the staples seen in the pictures was accomplished without the need for too much force. The only force that was applied was directed at the two staples in order to push them out of the tubes. The rotation out of the picture and advancement of the staples was automatic.

In an endolaminal application the staples would be pushed out of tubes that extend out of the body (a catheter). An expandable hinge or basket mechanism would be used to properly position the ends of the tubes against the vessel wall. This mechanism would also have the freedom to rotate.

Carlos Luis

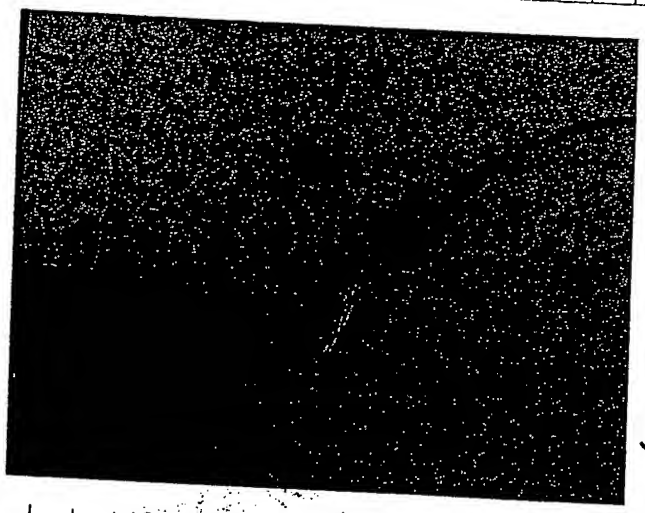
A prototype catheter of the design described on pages 22-26 was constructed. The following photographs illustrate its function.





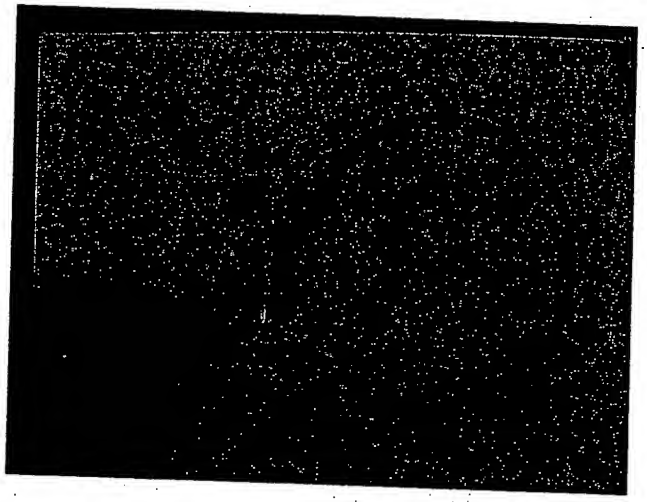
Close up of collapsed cage at distal tip of catheter.

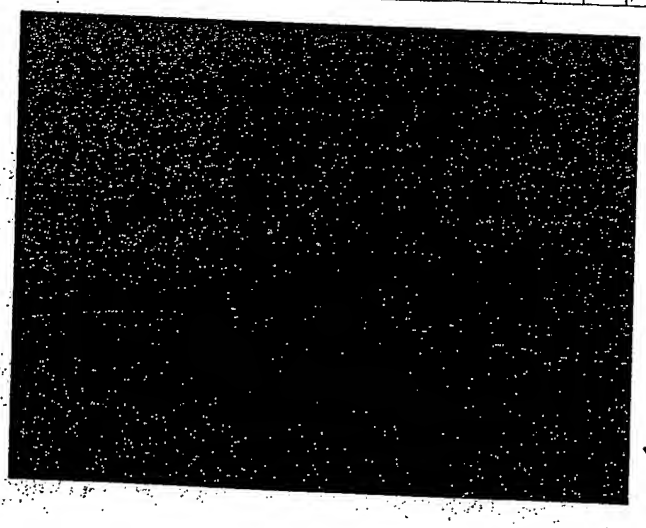
Close up of proximal end of catheter



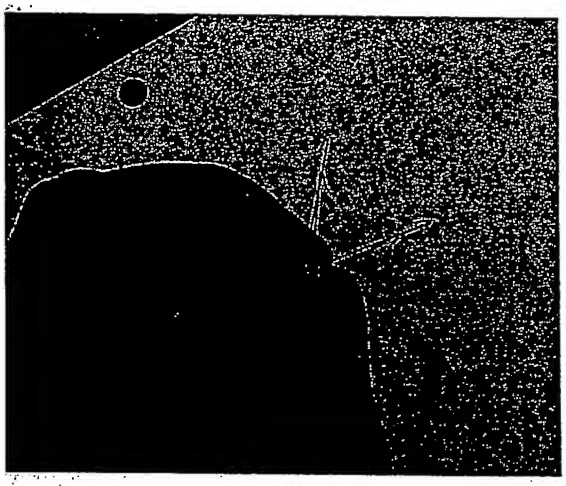
← expansion of cage actuated by pulling coaxial tendon tube

cage expands outward as tube is pulled. →



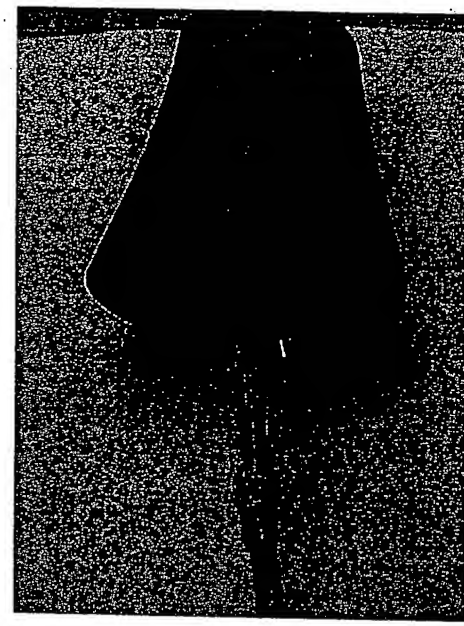


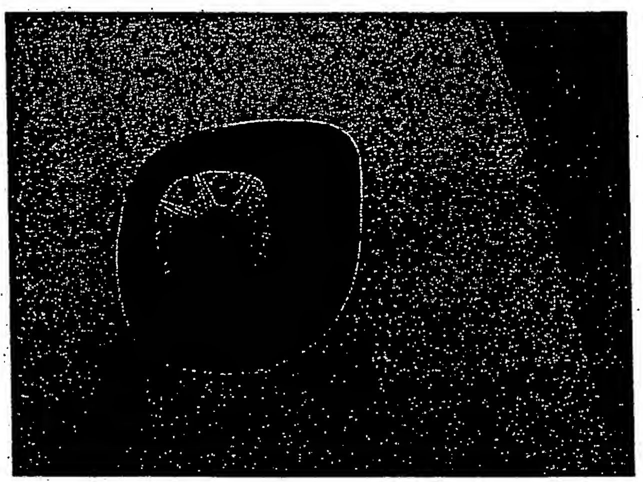
← close up of expanded cage. (side view)



← close up (end view) of expanded cage.

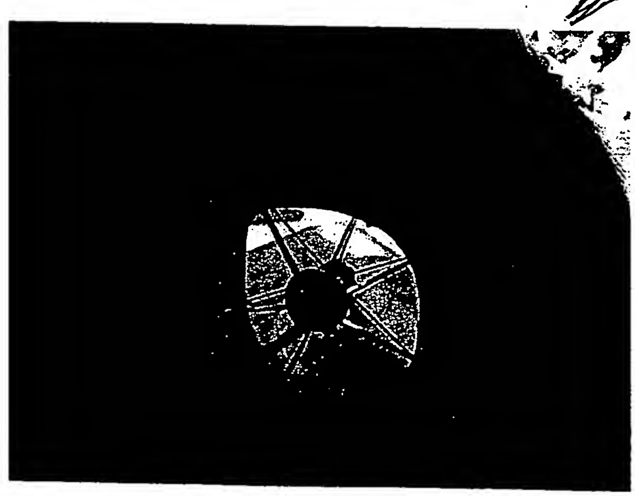
collapsed cage being introduced into collapsed tube →





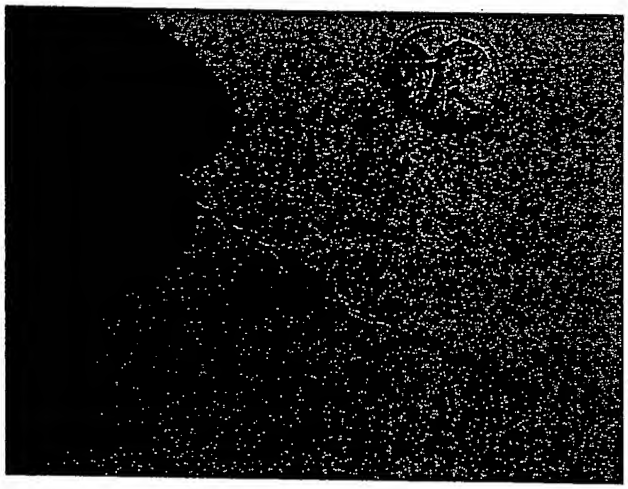
← cage expanded, causing tube to distend open.

expanded cage in tube. Dimples ~~against~~ ~~w~~ in wall suggest significant contact pressure. →

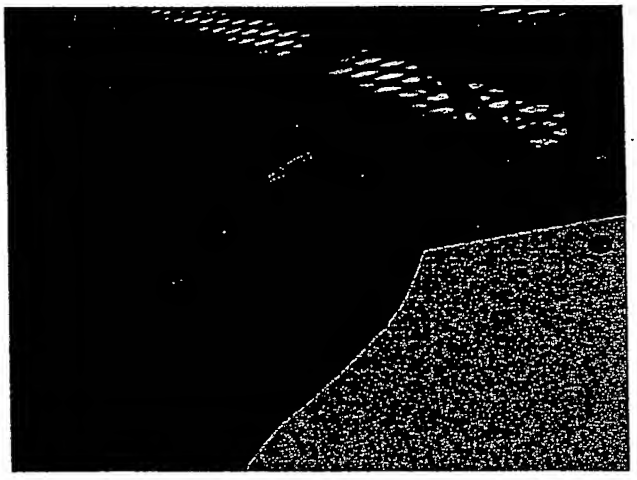


Staple for tissue closure

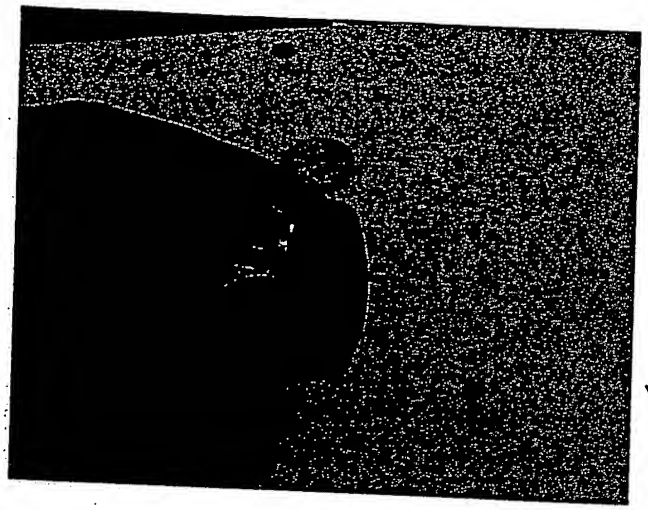
AN-11A staples were modified by cutting them and rejoining the resulting segments so that the barbs point toward each other. The resulting staples were then manually applied to surfaces of different shaped objects.



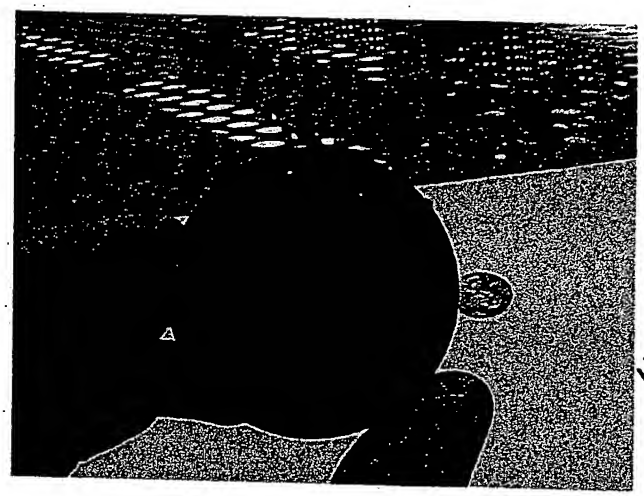
← Modified staple strip with barbs pointed toward middle



← 2, modified staples applied across ~~end~~ of bicycle inner tube in order to close tube openning



← end view of previous, showing staple strips across openning of tube



← Squash ball with segment cut out.

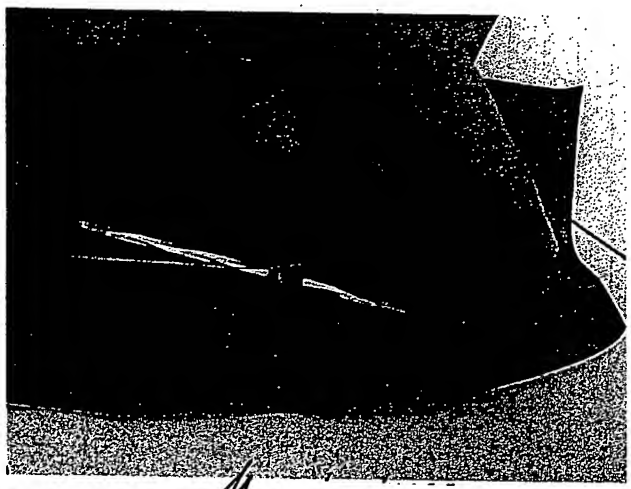
staple strip applied to ~~be~~ across openning of squash ball. Staple appears to be strong enough to hold openning closed

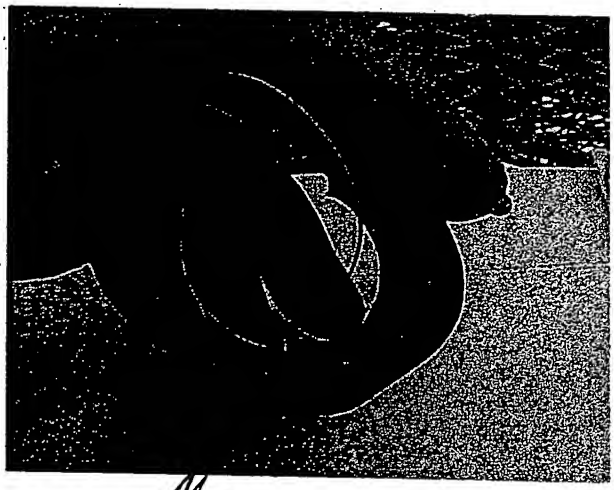
Mark Lee

Lily Kuo

Staple Suture Anchor

The modified linear staple (AN-11A based) described on pages 42-43 was evaluated as a means of anchoring suture to the inside of a hollow, elastic structure. A polyester thread was attached to the center of the staple. The staple was then manually applied to the inner surface of a bicycle inner tube.

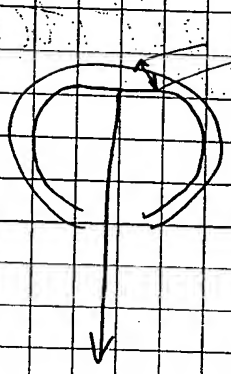


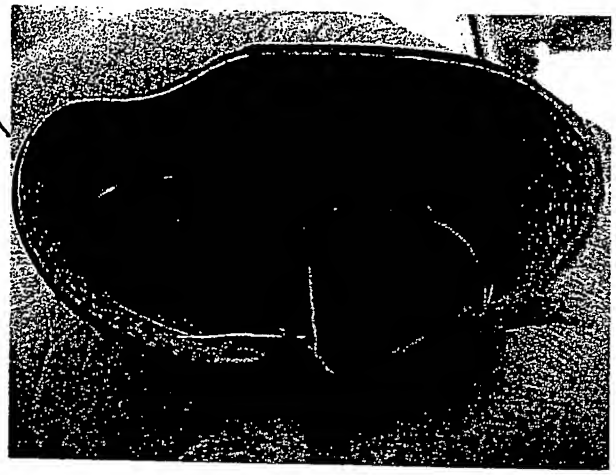


The bicycle inner tube was slit lengthwise first. After staple applica the thread was pulled through the slit.

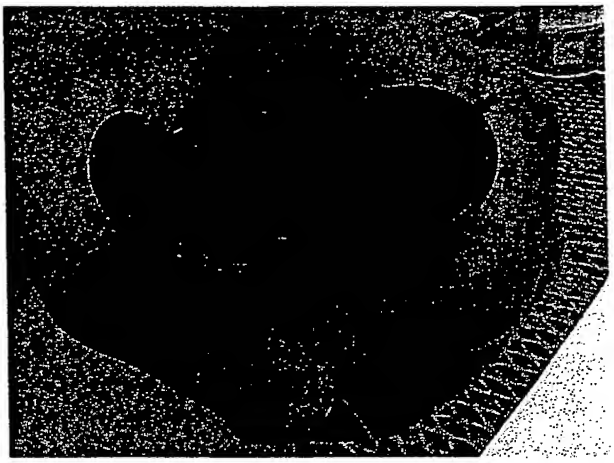
As tension on the thread was increased, the staple began lifting away from the tubing slightly at the attachment point of the thread. With fourth additional tension the staple and thread were able to pull the opposite tubing wall down toward the opposite wall. This suggests the potential use of the staple for closing or reducing the dimensions on body cavities.

← As tension as applied slight separation of the wall and staple can be seen.





← further tensioning collapses tubing further - anchors / barbs appear to be bending under the load by still remain embedded



← tube nearly completely collapsed by application of radial tension to staple.

One potential application of this may be in treating congestive heart failure by reducing left ventricular volume and/or wall stress by with the use of the staple and assembly.

Gayle Case / Betty Kam

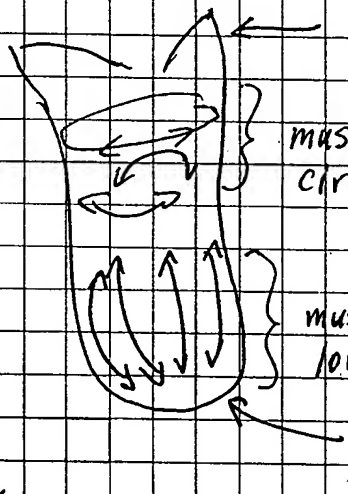
Method of Reinforcing Left Ventricle in Treatment of Congestive Heart Failure

Several literature references suggest that unloading or reducing wall stress in the left ventricle can be of benefit in treating congestive heart failure. Capouya et. al (Ann Thorac Surg 1993; 56: 867-71) suggest this in the context of a "girdling effect" of the latissimus dorsi in nonstimulated cardiomyoplasty. This is echoed in patients by Kass et al (Circulation 1995; 91: 2314-2318) based on their findings in patients who have undergone cardiomyoplasty. It was thought that a similar mechanical effect as that of a latissimus dorsi girdle could be achieved in a less invasive and traumatic procedure. Furthermore it may be accomplished endovascularly with conventional access and imaging means employed by interventionalists and surgeons.

To accomplish this a catheter would be used to implant a mechanism within the left ventricle. Access might be via a femoral approach through the aorta and aortic valve. The implant would be used to reduce the diameter of the ventricle or reduce its circumference or take some of the load off of the myocardium during diastolic filling and systole. This would be accomplished by adding reinforcing structures Endocardially in the ventricle or generally along the contours of the walls of the left ventricle. These implants may be circumferentially oriented around the perimeter of the left ventricle or longitudinally from the apix to the base. Based on literature (Streeter et. al, Circulation Research, Vol. XXIV, March 1969) it appears that myocardial

fibers are oriented mostly circumferentially, especially at the base and longitudinally at the apex.

One approach might be to introduce support in a direction consistent with that of the muscle fibers in the ventricle.



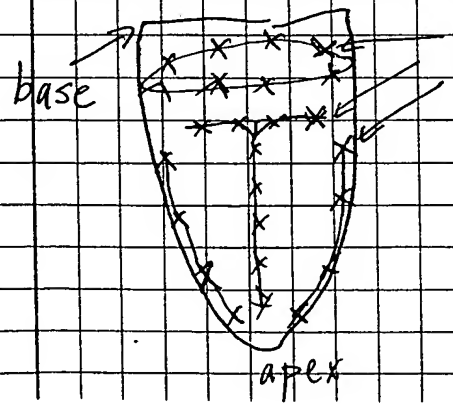
The reinforcement might do several things. It might act as a passive distention limiter on the expansion of the left ventricle in order to limit diastolic volume to its existing size. Alternatively, it might be used to reduce the dimensions of the ventricle and ~~maintain~~ limit its distention to the pre-set limits. As yet another

alternative, the reinforcement could be spring-like and always exert a force on the ventricle that would cause its dimensions to reduce. Finally, the same reinforcement can be actively driven by an energy source to cause it to act as a powered ventricular assist device.

The reinforcement structure may have many possible configurations. The common features of the designs are the attachment distributed attachment, flush along the endocardial wall in alignment with the predominant local direction of muscle contraction. Mechanical attachment to endocardial surface of the myocardium can be achieved through various means. Regardless of which means is used the reinforcement would rely on several attachment

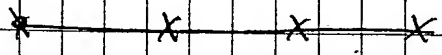
points to secure it along the path of contact with the epicardium. Between attachment points the reinforcing structure can be integral to the attachment mechanism or can be somewhat decoupled.

The reinforcing structure can be seen as a series of nodes (attachment points) that are interconnected. ~~Also~~ The nodes can be distributed in various configurations. It may be advantageous for them to ~~get~~ be distributed along the orientation of the local muscle alignment in order to ~~also~~ provide the most efficient mechanical support possible.

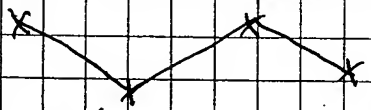


nodes - interconnected
- oriented with local muscle fiber orientation

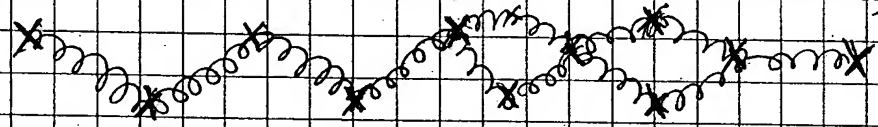
The nodes, or attachment points, can be in straight lines or,



zig-zags or combinations thereof.



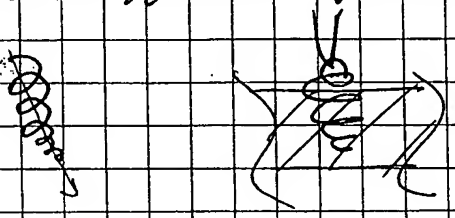
In addition they can be strung together with non-distensible string or a spring mechanism such as a coil. These can be sheathed,



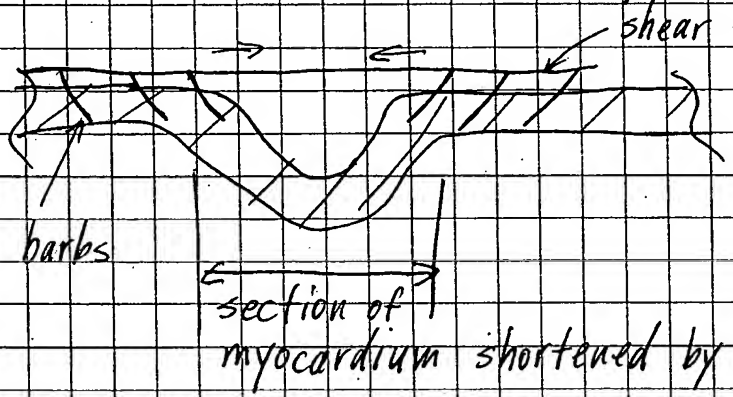
like bicycle cables, in order to protect them and also make them more "biocompatible".

Attachment mechanisms can have many embodiments. Ideally, they would need to be driven into and hold onto the myocardium without penetrating out to the epicardial surface. Cork-screw type endocardial

pacemaker leads are one possibility.

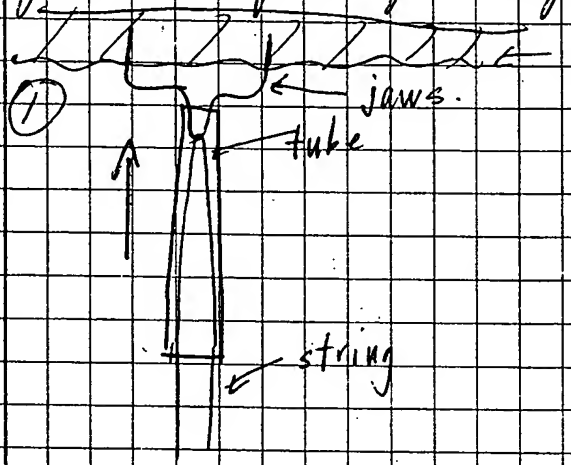


Or, shear strips such as the staples (AN-11A - modified) described on pages 42-46 could be used. Shear strips would have the advantage of low thickness against the endocardial wall and considerable shear strength in the direction in which they are aligned.

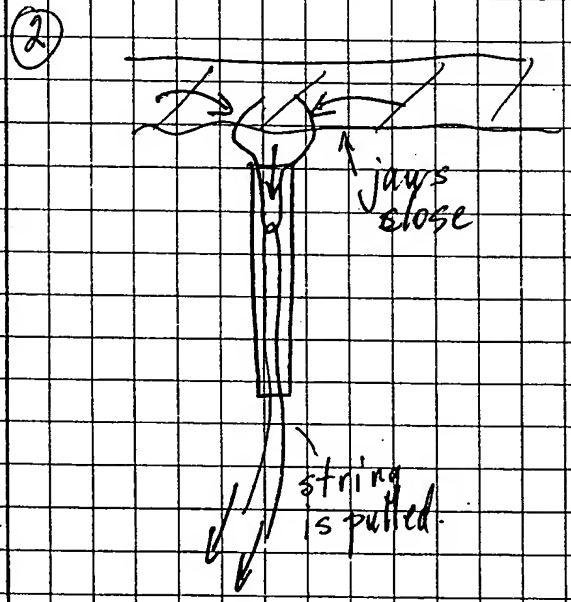


Alternatively, a punching anchor design might be used. This would consist of a set of jaws/barbs that would be applied to the endocardial surface. The base of the staple would then be pulled, causing the jaws to close. The

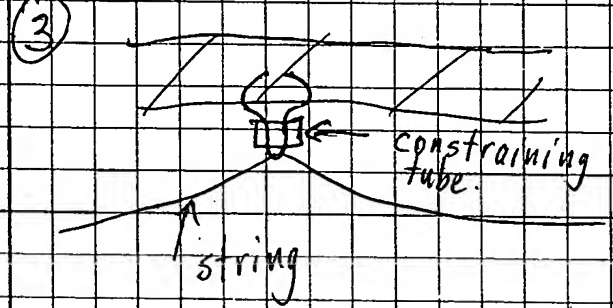
harder one pulls, the tighter the jaws squeeze together



Jaws are driven against or into tissue surface.



The string is then pulled, causing the jaw base of the jaws to slide into the tube. This causes the jaws to close and pinch the tissue between them.



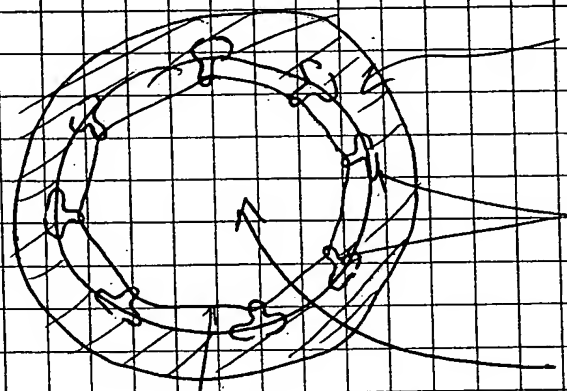
Finally a section of tube can be left behind to hold the "staple jaws" together.

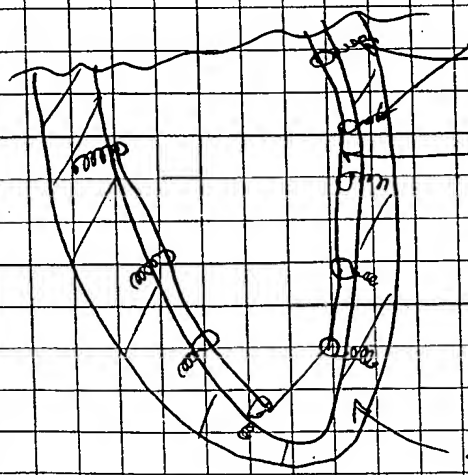
Sarah Lee

Lily Kan

Method of reinforcing myocardium

In continuation of the previous entry myocardial anchors or nodes can be implanted at desired locations and then in the left ventricle and then linked together similar with a string in a manner similar to the anchors and rope used by rock climbers.





The string can have adjustable length so that the physician can adjust the dimensions of the ventricle based on physiological data during the implantation procedure. Depending on the configuration of the nodes and connecting pattern of string between them the geometry of the ventricle can be altered to improve its function.

The ~~spring~~ string-anchor system may also be used to actively assist ventricular function. The system would be used like a series of pulleys to cause the ventricle to move in a way to lessen the work demand on the myocardium. An implantable power source could be used to actuate the motion of the string in the pulley system. ~~An~~

An important feature of these designs

as to have many nodes in order to distribute the loading on the ventricle wall and also mechanically couple a larger portion of the ventricle.

An alternative embodiment would involve the use of spring-members to link the nodes. ~~This might~~ If the springs have a preload that causes them to contract the myocardium ventricle, the contractility and pumping efficiency might be improved. In addition, the springs might relieve load on the muscle wall by carrying tensile loading, much as the carbon fibers would in a carbon fiber-epoxy matrix composite material. This might be accomplished with the shear strips mentioned earlier as well.

Paula

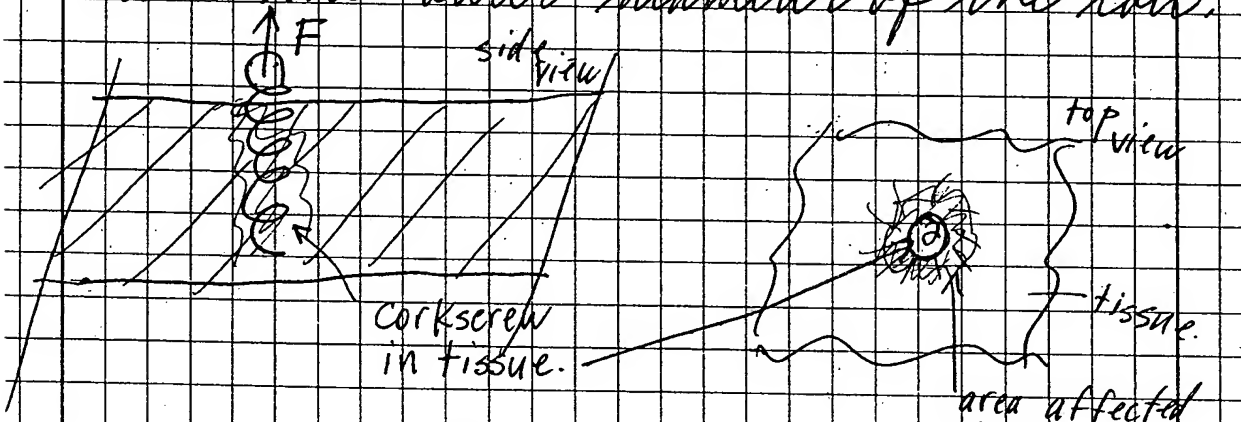
Dilip Rao

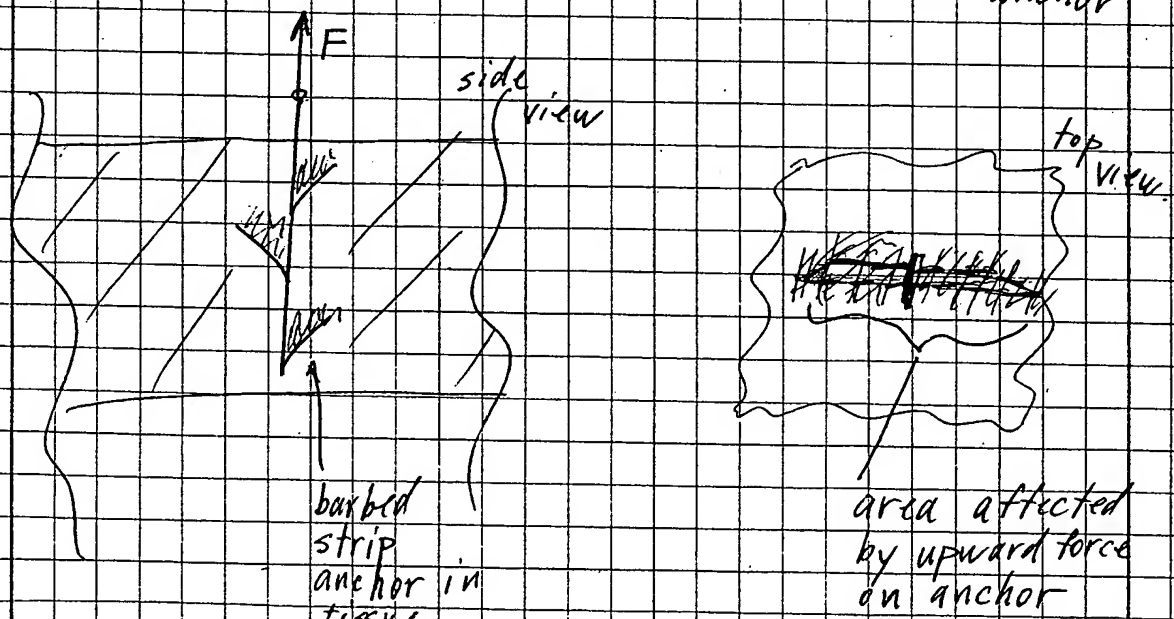
Tissue Anchor Designs for Endocardial LV Harness

Two different tissue anchor designs were evaluated for use in anchoring an endocardial left ventricular harness as described on pages 47-57. The first design consists of a wire coil which would be screwed into the myocardium much as a corkscrew would be driven into a cork. The second design consists of a flat strip of metal from which barbs extend outward in various directions.

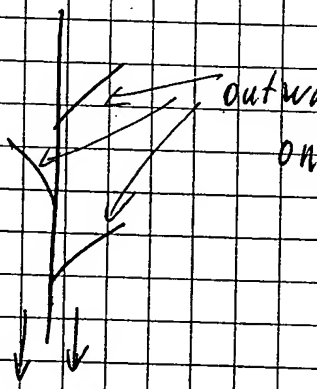
Both designs would be delivered endovascularly through a catheter. The corkscrew design would be pushed as well as turned in order to cause it to advance into the myocardium. The barbed strip design would simply be pushed into the myocardium.

anchoring or resistance to pull-out from the myocardium would be achieved in different ways. The entire length of corkscrew would push against tissue. The volume of tissue that would feel this would be confined to the area near the outer diameter of the coil.





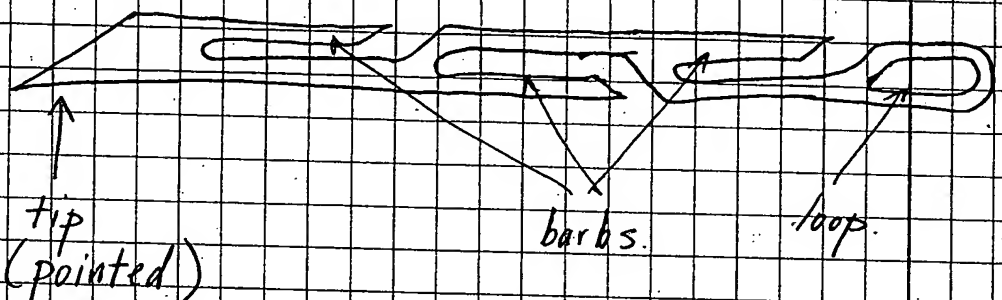
The barbed strip anchor would rely on the barbs the to bend away from the spine, so that anchoring force would be dependent on the length of the barbs and their ability to reach outward and engage as much tissue as possible. The staple design (AN-11A) can be modified so that it can be used for this application. To do so the barbs would be bent outward.



The staple would be loaded into a tube and pushed out xx of it when it is driven into tissue.

A loop at the end of the staple

would allow a series of these anchors to be strung together into a network. Such an staple anchor might look like the following:



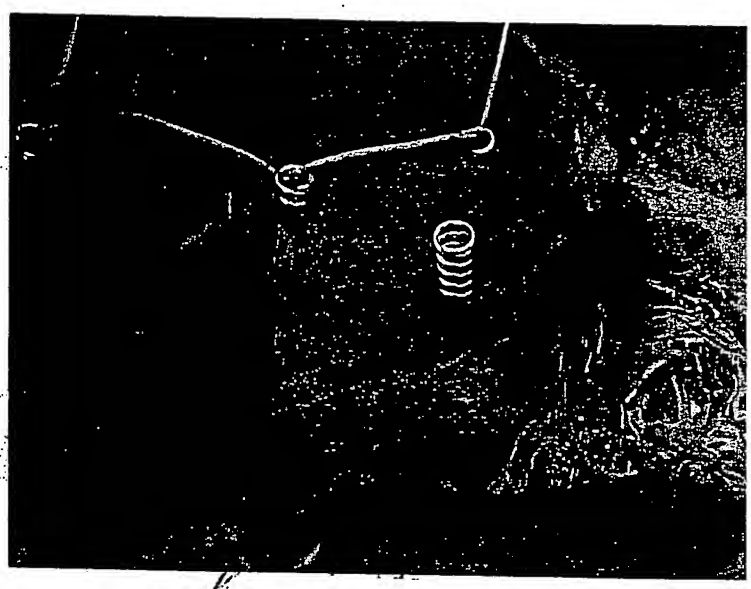
The anchor wouldn't necessarily have to be flat with barbs projecting outward in a single plane. The spine of the anchor can be twisted so that when bent, the barbs project outward in many directions. This might increase its traction in tissue. Another way of increasing the pull out force is by increasing the number of barbs along per length of anchor.

Paula Can / Robyn Kan /

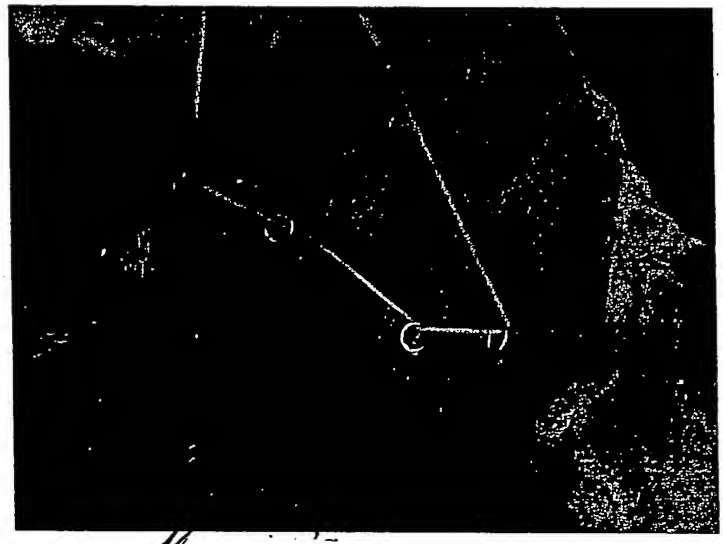
Evaluation of Endocardial Harness System in Porcine Ventricle

The concept of an endovascularly implanted endocardial harness to reduce myocardial wall stress was evaluated in a fresh pork heart. The harness consisted of anchors or nodes and a thread that is slideably connected to each anchor. Cork screw / coil anchors were used in this evaluation. The cork screws were manually driven into the endocardial ventricular surfaces by twisting, like a corkscrew used to open a wine bottle. Surprisingly, little torque or force was required to thread the coils into the tissue ab 1 cm. deep. Once in place, the coils were surprisingly secure. Attempts to pull them out showed they were able to resist the application of proba several pounds of force.

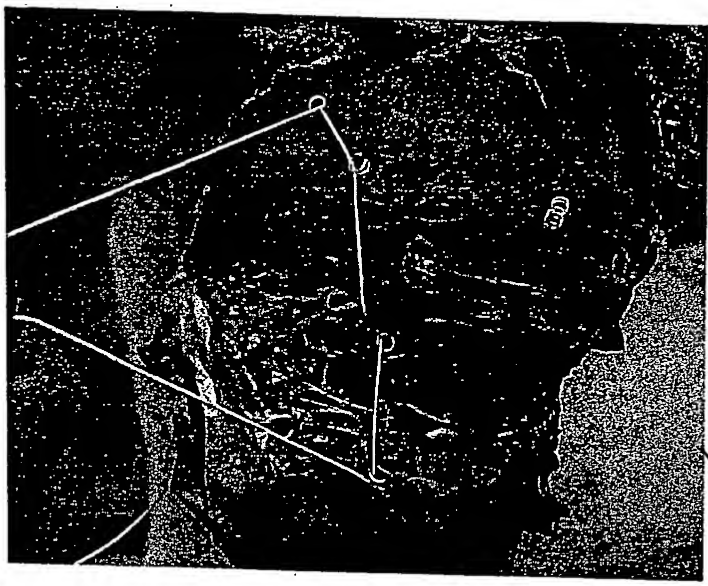
Once the corkscrews were driven into the tissue until very little coil remained above the surface a polyester thread (Poly-Tape 2016 backing) was threaded through the tops of the corkscrew anchors in a continuous fashion. The ends of the line were then brought together and used to lift up the heart. This lifting by the line caused the previously flattened heart to assume a curved configuration more like its natural state before being sliced open. The anchors/ corkscrews did appear to be close to dislodging under this load. The thread appeared to lay very flat and flush against the ventricle wall, even when traversing trabeculations, under this tension. The following photos illustrate these points.



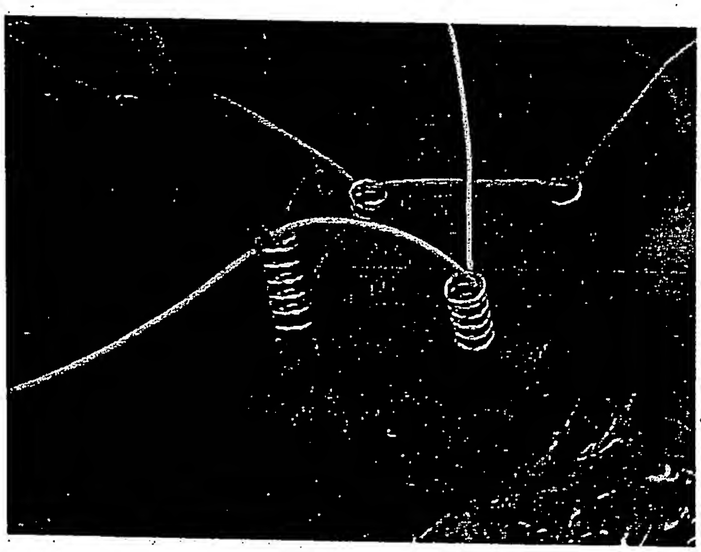
Cork Screw anchors screwed flush into myocardial surface and slideably tethered by thread



Sliding thread crosses over muscle (papillary) feature. Thread remains flush against surface.



flattened, heart (sliced open) with corkscrew harness in circumferential orientation with respect to heart wall.
Only slight tension is being applied to strings



Close-up of corkscrews (photo out of sequence.)

Follow up to photo at top of page. Heart is lifted by strings via anchors. Resulting tension in string causes heart to close ~~somew~~ noticeably from flat configuration.
Also, anchors appear to remain secure. Slideable attachment to coils creates even tesion between nodes.

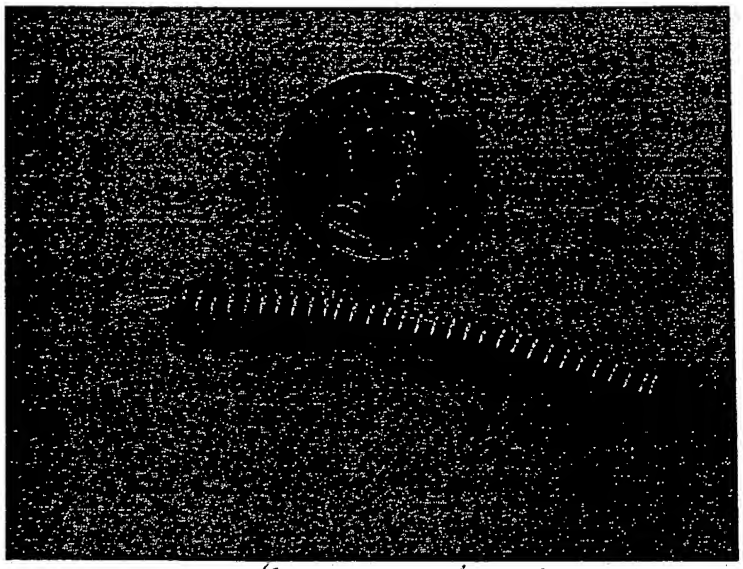
[signature] [signature]

Method of Making Creating Steerable Thread Harness System

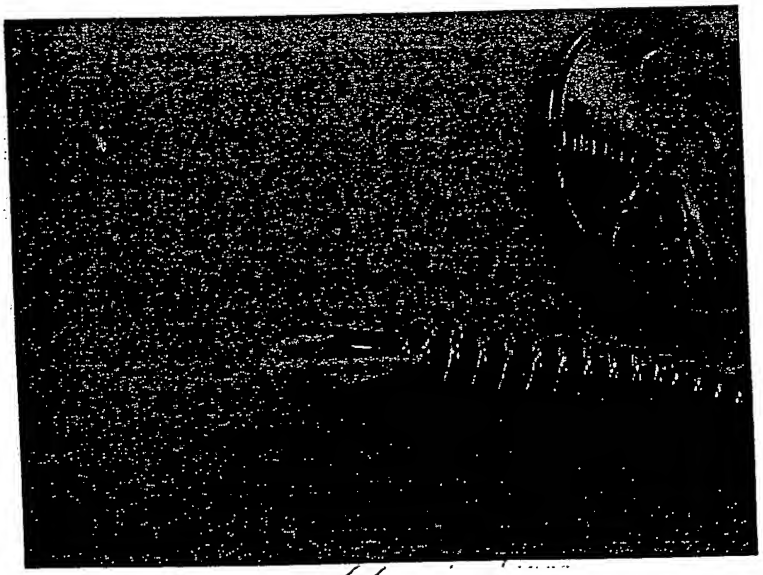
The following is a method by which a steerable harness system can be created. As described earlier in this book a system comprising a series of corkscrew tissue anchors interconnected by a slideable thread may be useful for harnessing the walls of a vessel such as the left ventricle. This entry describes how a series of slideably tethered corkscrew anchors can be delivered at the end of a catheter.

In the following sequence of photos a series of 3 identical corkscrew coils are slideably mounted over a catheter shaft with several lumens. A string is threaded through one of these lumens. At the one end (the distal end) the string ends in a loop. The distal end of the distal

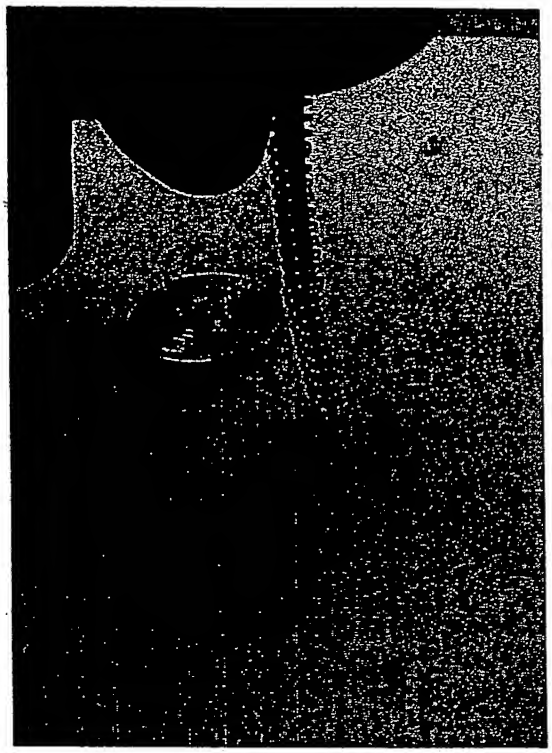
most coil is threaded through the eye of the loop.

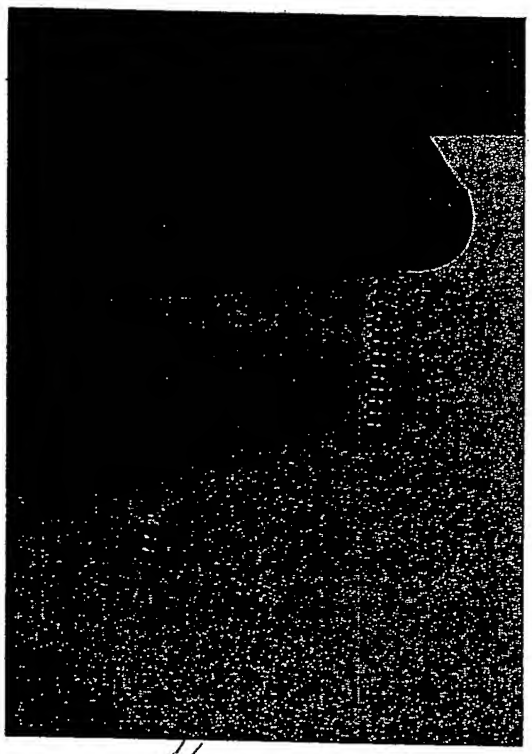


← 3 coils at end of catheter. string extends out of lumen at catheter tip. String then engages coil by means of loop.



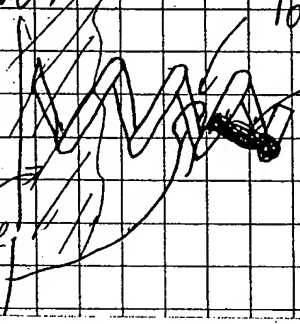
← Close up of loop of string threaded over end of coil.



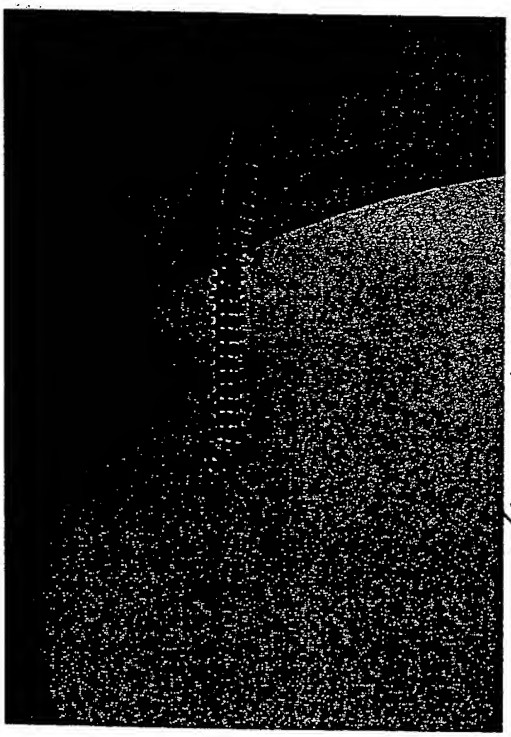


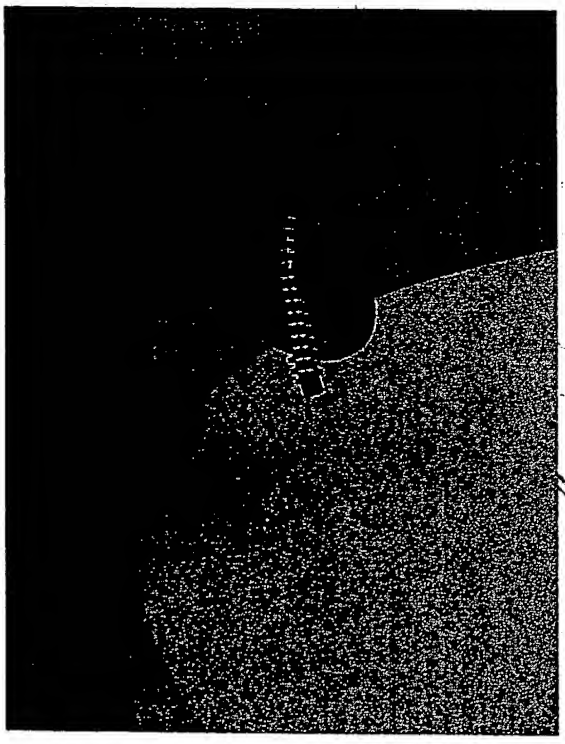
The distal tip of the catheter was then positioned against a piece of foam (in order simulate tissue. The cork screws were then turned to cause the distal-most screw to bite and dig into the foam. As the cork-screw advances into the foam the loop of string remains at the surface. In other words the windings of the coil pass through the loop as they wind into the foam. When the screws are advanced to their desired depth the catheter tip is lifted away and advanced to the location of the next screw placement. The fact that the string is threaded the central lumen slideably allows

the next screw to be placed wherever the operator desires. The coils in this demonstration are not closed at their back ends. Ideally, they would be to prevent the loop of string from disengaging from them.



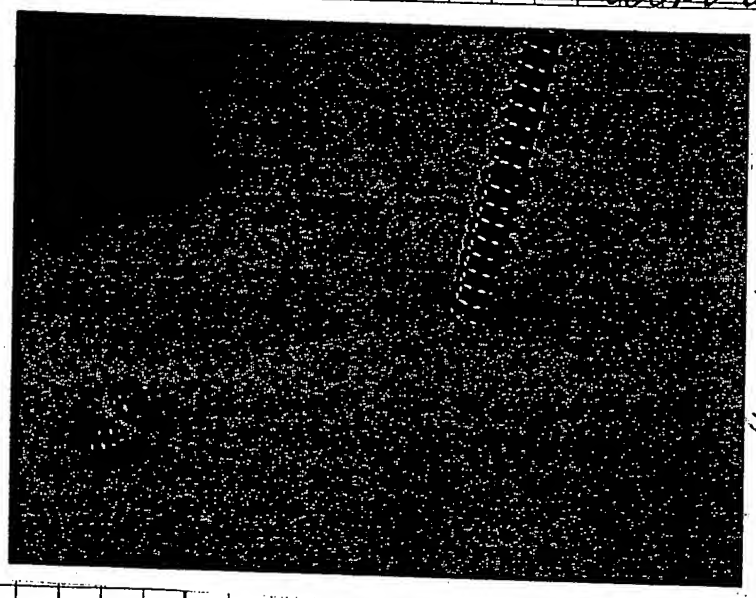
closing of coil (i.e. with solder) to prevent loop from separating from coil



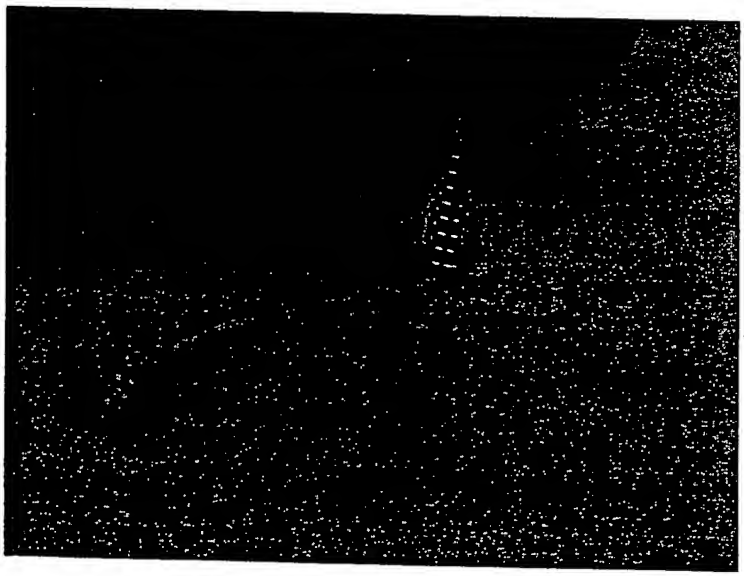


Close up photos of completion of and lift off of catheter from first coil after its insertion. (These 2 photos appear before the previous one [page] chronologically).

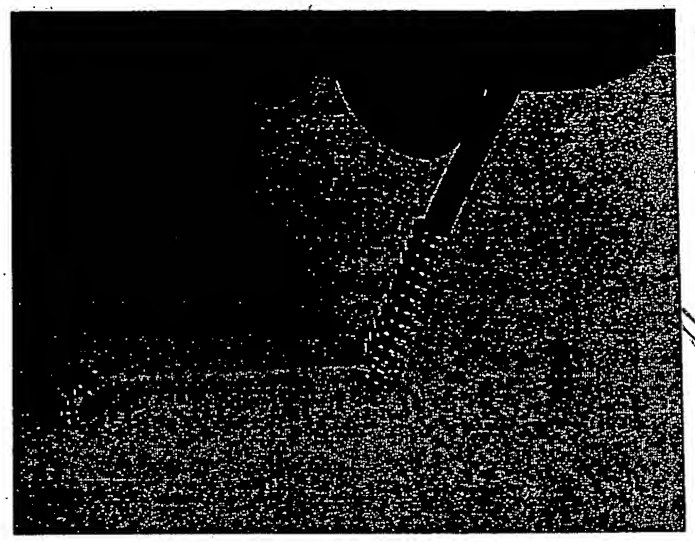
As the second coil is driven in it is forced to engage the string as it extends over from the first coil. Thus, as the second coil twists the string slides up along the coil and remains at the surface as the coil winds deeper into the tissue.



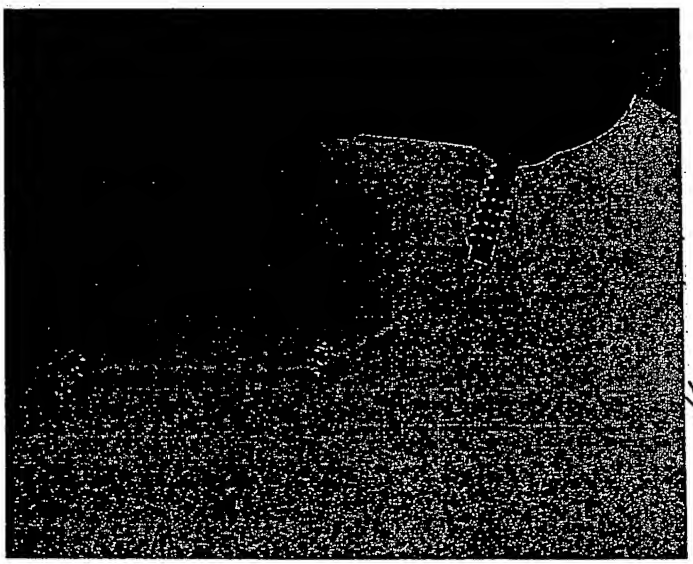
← second coil engages string between wind



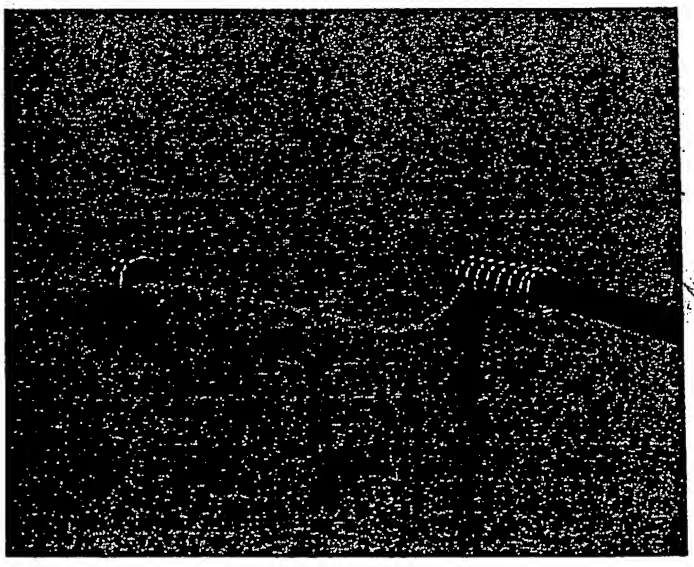
← second coil as wind dig deeper into tissu String remains at t surface as coil is screwed in further.



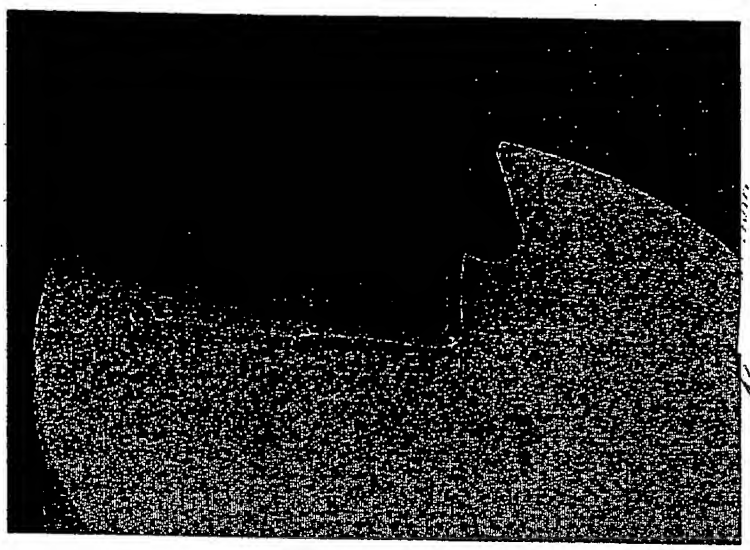
← second coil threaded into tissue, prior to removal of catheter. (String remains at surface). As with first coil, string remains threaded through winding, although without a loop.



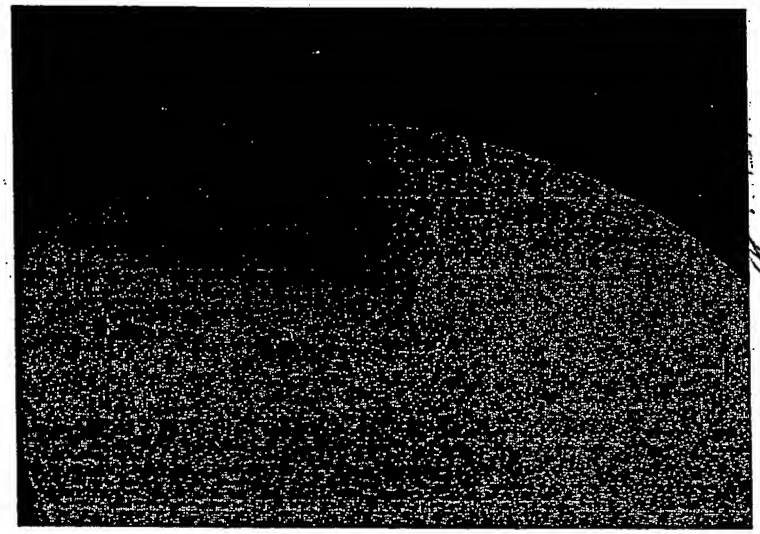
← catheter advanced to location of third coil. Slideable coupling to second coil is seen. Second coil would also be closed with solder, etc. to prevent separation



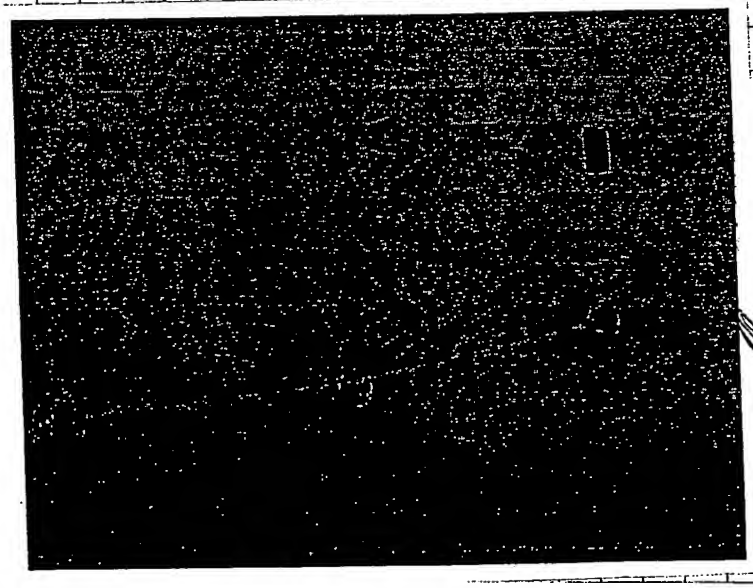
← Third coil being threaded into tissue. Again, string remains at surface as coil winds by.



← Completion of placemen
of third coil



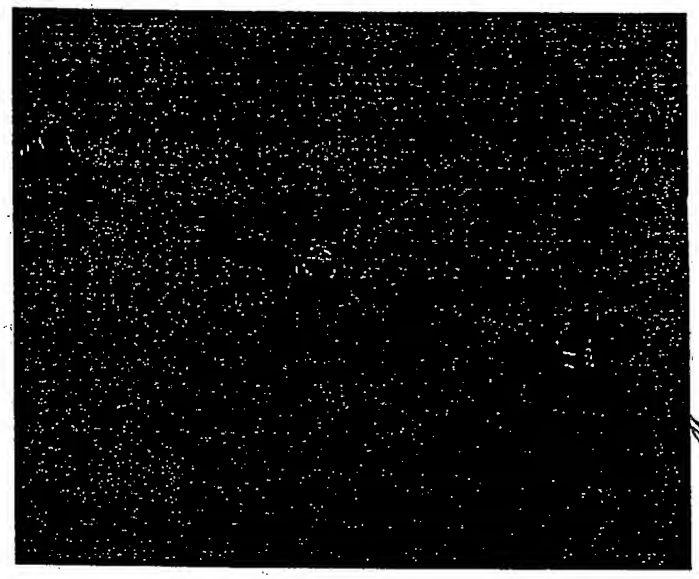
← Lift off of cathete
from third coil.



← Plastic plug is then
slid over string to
last anchor point.

Tension can then be
adjusted. Then,
based on physiologica
feed back, tension c
be locked in by

advancing knot to hold plug in place. The string would then be cut.



← plug locked in placed by knotted string. Desired tension in string is thus maintained.

It should be noted that not all available coils need to be implanted. With this system the array of tethered anchors or harness can be terminated even if not all coils on the catheter have been implanted. In addition string tension is evenly distributed between coils via the slidgate coupling between string and coil.

Paul Carr

Tulip Tran

Oct. 11, 1999

Active Systolic Mechanical Assist

If the left ventricular wall can be harnessed with the system shown in the previous entry it may be possible to provide systolic mechanical assist. The steerable coupling between string and endocard anchors would allow the distance subtended by the anchors to be actively changed by changing the tension on the string. In essence the myocardium would be like a puppet controlled by strings. The strings can be enclosed by a jacket to minimize abrasion. ~~After~~ From the inside of the left ventricle, the strings can be extended outside the heart via a hole in the apex or trans-septally out the subclavian vein as is done in transvenous pacemaker lead placemen

Oct 21, 1999

Once outside the heart the strings can be connected to an actuator. This can be powered by a battery powered energy source. Alternatively, it may be powered by the patients themselves. For example, mechanical energy may be harnessed from the diaphragm during breathing and stored in a mechanical reservoir such as a spring. Energy from the reservoir could then be diverted to the ventricular harness strings. Timing of contraction could be gated so that energy from the reservoir is released at the right time and amount.

In addition, the harness may be used for electrical mapping, pacing, or defibrillating in addition to the mechanical functions described here.

Paula Lee 10/19/99 / Kelly Lee 10/11/1999

Oct. 25, 1999

Cardiomyoplasty: Harnessing of the Left Ventricle

The following is a description of how the harness (myocardial) as described previously in this book can be used to slow, halt or reverse the progression of congestive heart failure.

Others (Capanya) have suggested that clinical improvement in heart & fault failure can be brought about by passively girdling the heart with latissimus dorsi muscle. Although this doesn't cause a reduction in LV diastolic volume in itself, the it likely would carry much of the load, much as the carbon fibers would in a carbon-fiber-epoxy composite structure. This would reduce wall stress or tension in the myocardium and reduce its energy usage. Overall the "physiological stress" on the LV

would be reduced.

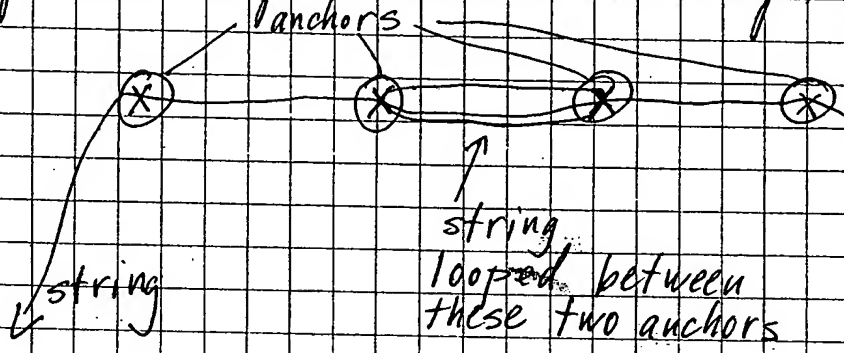
Further benefit may be achieved by actually reducing the size of the left ventricular circumference in addition to restricting the extent to which it can expand.

This may be accomplished using the harness described earlier. After the last anchor has been imbedded into the myocardium the harness can be tightened by pulling on the string. Real-time physiological parameters may be used to determine the appropriate tension based on reduction of LV diameter and accompanying physiological changes. Once the desired harness tension has been found, the string would be tied off at the last anchor. Finally, the string would be cut.

If desired varying amounts of

Oct 25, 1999

strain relief in the myocardium can be achieved by looping the string between anchor points to create a pulley effect. This might be used to compensate for varying rates of strain in different portions of the myocardium during ~~during~~ ejection.



When the string is pulled or tensioned the loops between anchors cause the anchor points to come closer together. However, the more loops there are, the less motion is achieved per given length of string pulled. In areas where there is less myocardial stretching during the cardiac cycle it may be desireable to loop the string between anchor points more than between

anchors where there is less stretching/shortening.

Ideally, the harness would be placed in alignment with the direction where there is most shortening or lengthening of the myocardium during the cardiac cycle. Some have suggested myocardial fibers are oriented in a helical configuration in the left ventricle. (Streeter). If this is the case the harness would best be placed in a helical configuration ~~xx~~ either on the endocardial or epicardial surface. The harness string would be long so that it does not affect the initial compliance of the LV during diastolic filling. Once a certain diastolic volume has been reached the string/harness prevents the LV from filling further by limiting

its circumference, and increase in effect increasing decreasing its compliance without requiring more work of the myocardium. During systole, the LV would contract unencumbered by the harness. The harness would simply buckle and go slack until the LV is filled again during diastole. In essence, this passive application of the harness would be a diastolic assist. As mentioned previously this diastolic assist can be augmented by systolic assist by powering the string.

Both endocardial and epicardial placem have foreseable advantages and disadvantage An endocardial system would be placed with a catheter on the endocardial surface of the left ventricle. Placement of the anchors may be difficult because of the intraventricular anatomy / morpho trabeculae, papillary muscles and, chordae

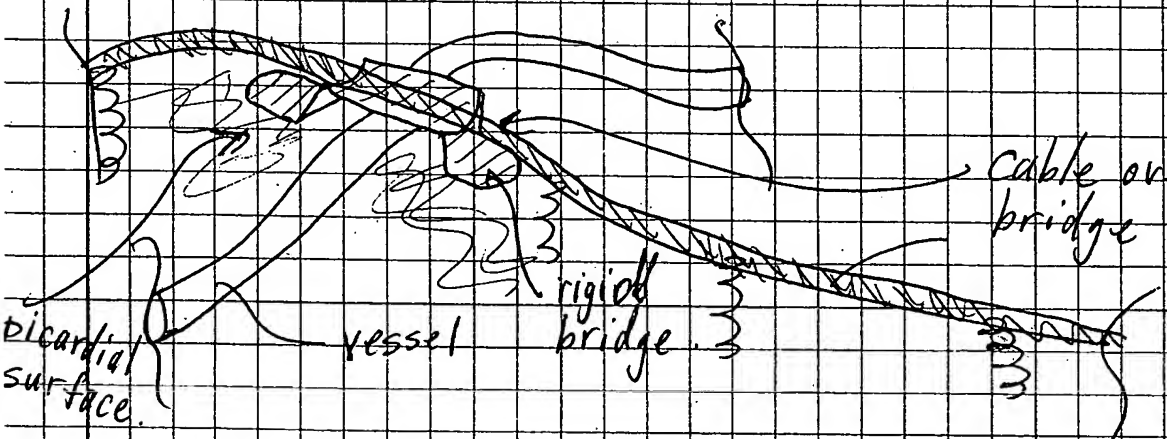
may interfere with placement and secure anchoring as well. The harness apparatus may be a nidus or source of thromboemboli which would be especially dangerous given that they would enter the aorta. The anchors themselves would ~~have a~~ be under a load which would pull them outward from the myocardium. However, an endocardial placement would allow a very-non-invasive percutaneous placement. In addition, the endocardial harness would not interfere with the epicardial surface in particular, the coronary arteries and possibly bypass grafts. Lastly, stress analysis of thick walled vessels suggests the presence of significant radially directed compressive loads in the LV. These loads are maximal at the endocardial surface. Some of this load

Oct. 25, 1999

may be relieved by inwardly directed load, such as that from that can be generated by an endocardial harness. A possible result might be improved perfusion of the myocardium via lowering of pressure. An epicardial harness might be placed through an open surgical procedure or minimally invasively via a thoracotomy. Placement of the anchors would be easier because of more direct access. The harness would not come in contact with blood. This reduces the chance of a thromboembolic complication. The anchors would not have any ~~load~~ an outward, relative to the epicardial surface, load on them. The string/cable of the harness would be directed inward toward the LV cavity. The placement of the harness would not interfere with existing

Oct. 25, 1999

bypass of or future bypass grafts, unlike the situation with a latissimus dorsi wrap. This is because the anchors and cable/string would take up very little of the epicardial surface. If coronary arteries or bypass grafts need to be traversed a prosthetic ~~for~~ bridge can be attached to the epicardial surface in order to route the cable over the vessel without compressing the vessel.



Finally, if the cables and harness are to be actively driven by a power source access would be much simpler if the harness were epicardially placed.

Carlos Cau 10/26/99 / Dilip Das 10/25/1999

Oct. 25, 1999.

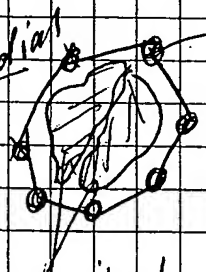
Mitral Valve Repair Using Harness

Mitral valve regurgitation resulting from ventricular enlargement often is due to a lack of leaflet coaptation. In addition to valve replacement, valve annuloplasty or reinforcement is used to bring the valve leaflets closer together.

An harness system, such as the one described previously in this book, can be used to bring the leaflets back in contact or coaptation. The harness / anchors would be placed around the annulus of the mitral valve and then tightened. ~~to the~~ This can be accomplished endocardially leaving a surface-flush harness across the mitral valve. Via an epicardial approach, a semi-circular, circumferential (relative to LV long axis) harness can be placed around the base of the LV and tightened to bring the leaflets into

Oct 25, 1999.

contact.



Sandra Lan 10/26/99

Dilip Tam 10/25/1999

Oct. 27, 1999

Harnessing Patterns for Left Ventricle

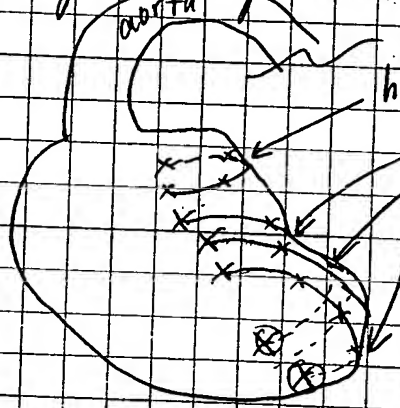
The following outlines possible patterns for epicardial or endocardial harnessing of the left ventricle for either passive or active constraint of the chamber. These patterns are meant to treat various forms of congestive heart failure. The passive harness can be used to treat dilated cardiomyopathy by reducing ventricular volume and/or wall stress. In addition it can be used to treat mitral valve regurgitation. The actively driven harness can be used to treat these diseases as well and also ischemic cardiomyopathy by assisting ventricular contraction.

For both active and passive harnesses the idea would be to place the harnesses in the direction of myocyte fiber orientation or contraction. It would be the orientation that undergo

Oct. 27, 1989

the most elongation or strain. Alignment with this orientation would optimize the efficiency of the harness. It has been suggested that the left ventricle contracts in a twisting or wringing motion that roughly resembles a left handed helix. This is corraborated by the findings that myocardial fibers are oriented as such.

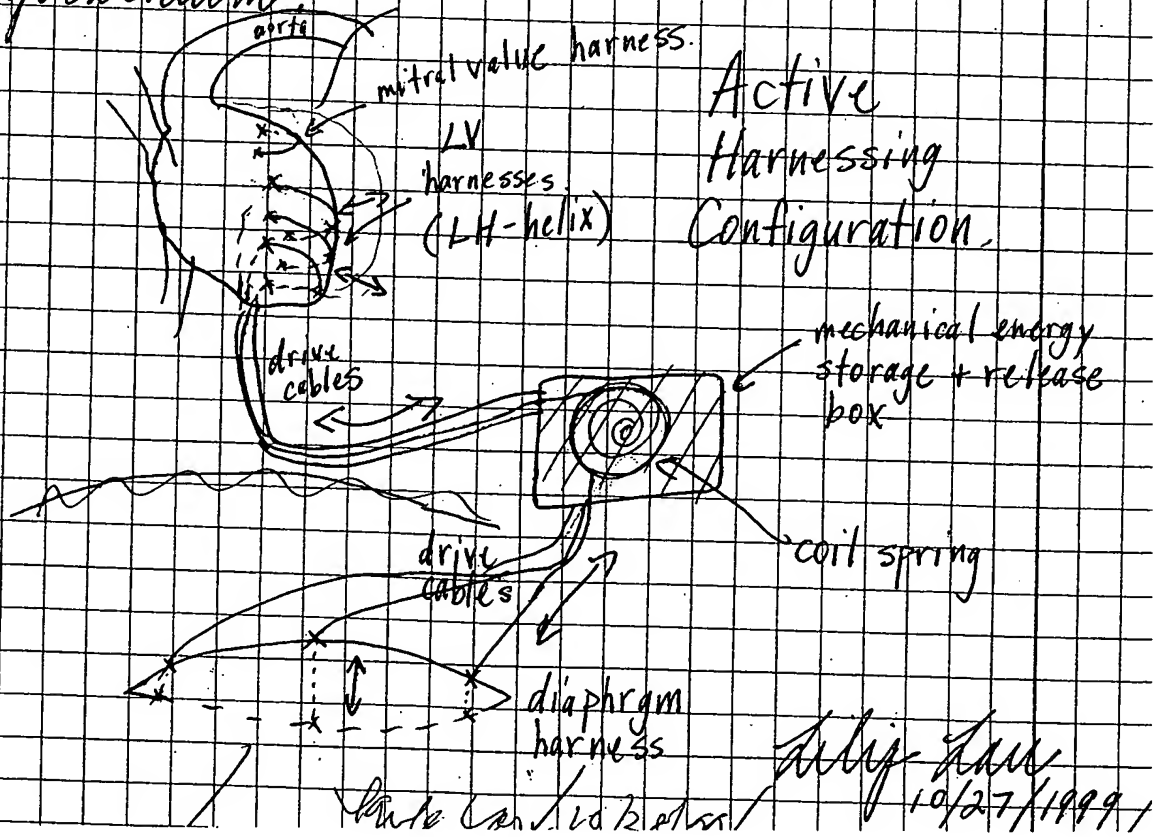
Accordingly, the most mechanically efficient method of reducing the workload of the left ventricle would be to reduce apply mechanical support, actively or passively, along this orientation.



Passive Harnessing Configuration.

Oct. 27, 1999

Several harnesses may be anchored, as shown in the sketch, around the left ventricle, endocardially or epicardially. These would extends from one septal edge around the chamber to the opposite edge of the ventricular septum. The septum itself may be a very good segment of myocardium for mechanical anchoring because longer anchors may be imbedded without going penetrating the far edge of the myocardium.



Active Harnessing Configuration.

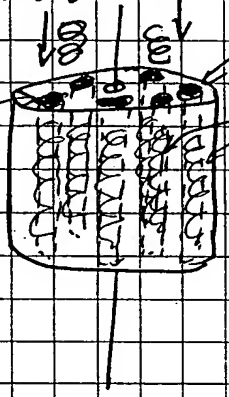
Abby Lau 10/27/1999

Revolver-Magazine for Harness Anchor Delivery System

Oct. 27, 1994

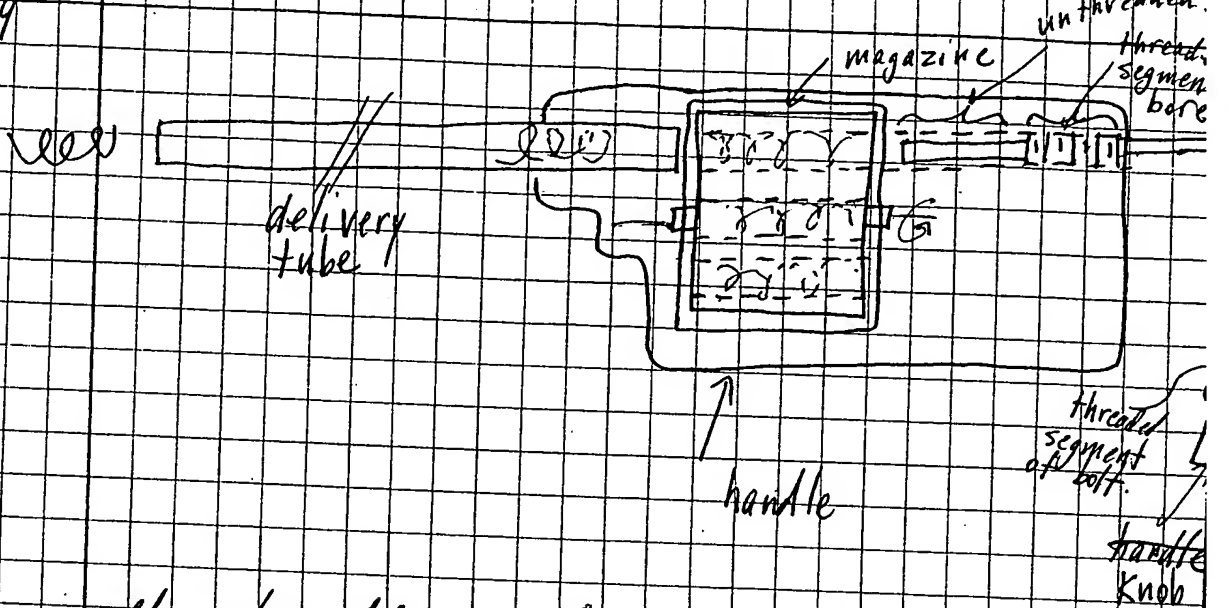
The following describes a mechanism that allows rapid placement of a plurality of myocardial anchors to create a harness. The system would consists of several parts: a delivery tube, a handle or housing, a rotating magazine, anchors, a cable, and a bolt.

Corkscrew anchors would be loaded into a rotating magazine, like those used in revolvers.



The magazine would be aligned with a delivery tube through which the anchors would be pushed and screwed out. Both would be set in a handle/housing. At the opposite end of

Oct. 27, 1999



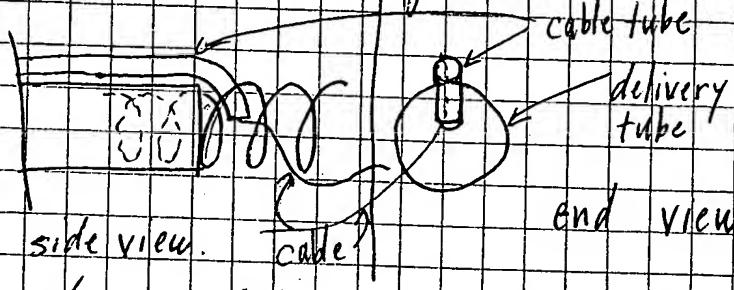
the handle a bore would extend back from the the magazine. The bore would be threaded partially, lengthwise, near the back end. A ~~bolt~~ ~~a~~ torquable, sliding bolt would be inserted sidearly through ~~the~~ this bore, through the anchor bores of the magazine and through the delivery tube. In doing so an anchor would be pushed or advanced to the tip of the delivery tube. At this point the thre portion of the bolt would come in cont with the threaded portion of the handle t This would prevent further translation of the bolt and anchor forward. At this point the ~~handle~~ bolt would be screwed forward into

the handle causing the bolt to twist forward. The bolt would engage the anchor at the tip of the delivery tube and cause it to screw forward out of the tube and into tissue. Once this has been completed, the bolt would be unscrewed out of the handle and pulled back out of the magazine bore. The magazine would then be rotated to advance the next bore containing an anchor in position. The bolt would then be advanced through this anchor containing bore, in doing so the next anchor would be pushed out of the magazine and down the delivery tube to be screwed into tissue. This would be repeated until a satisfactory number of anchors has been placed.

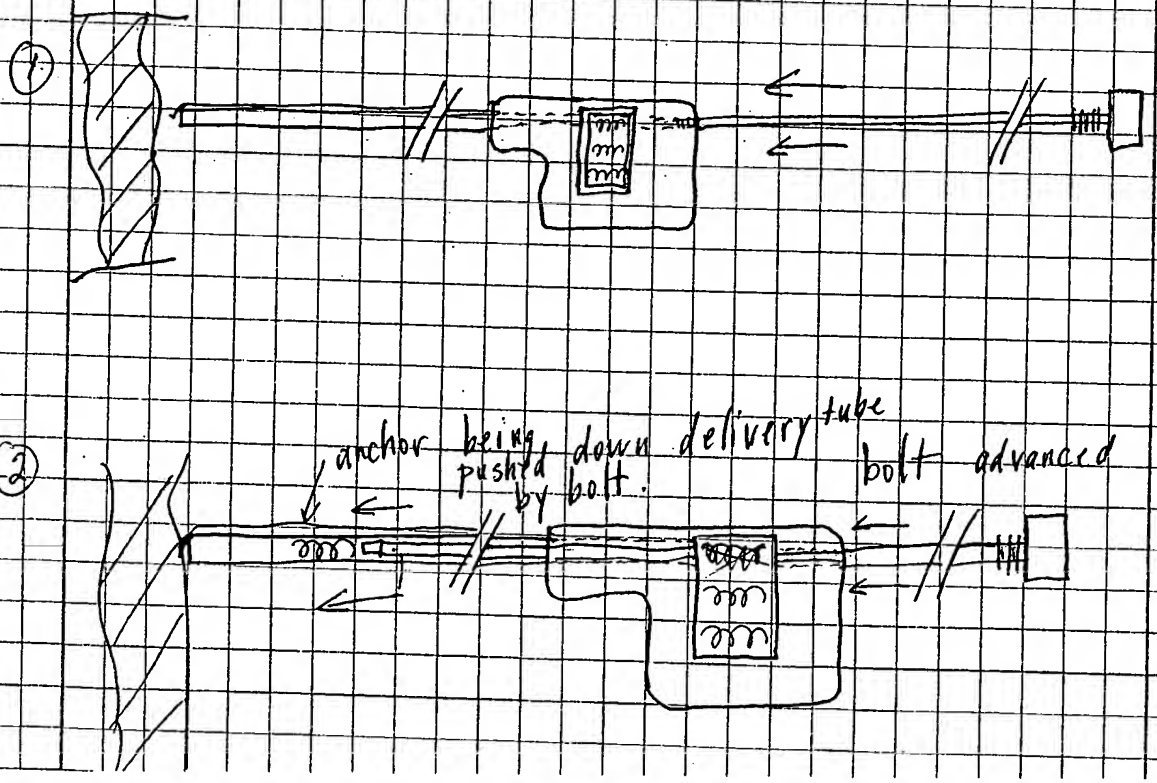
If it is desireable to link the anchors via a string or cable or secondary tube, containing the cable would extend

Oct. 27, 1999

alongside the delivery tube to its tip. At the tip the end of the cable tube is would bend inward into the lumen of the delivery tube. This allows

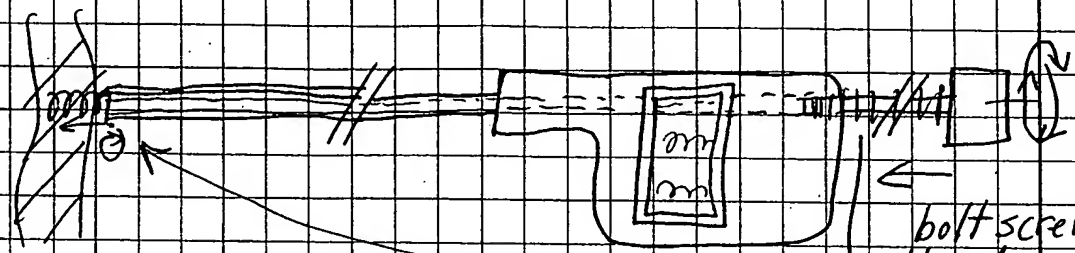


the cable to catch into the windings of the anchors and be threaded up the anchor as discribed on pages 66-73 of this book.



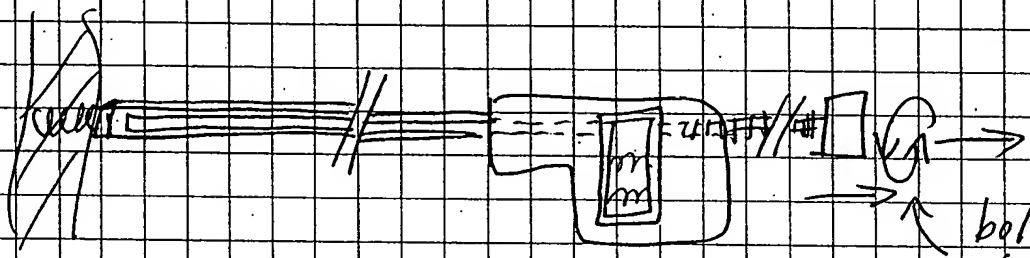
Oct. 27, 1999

③



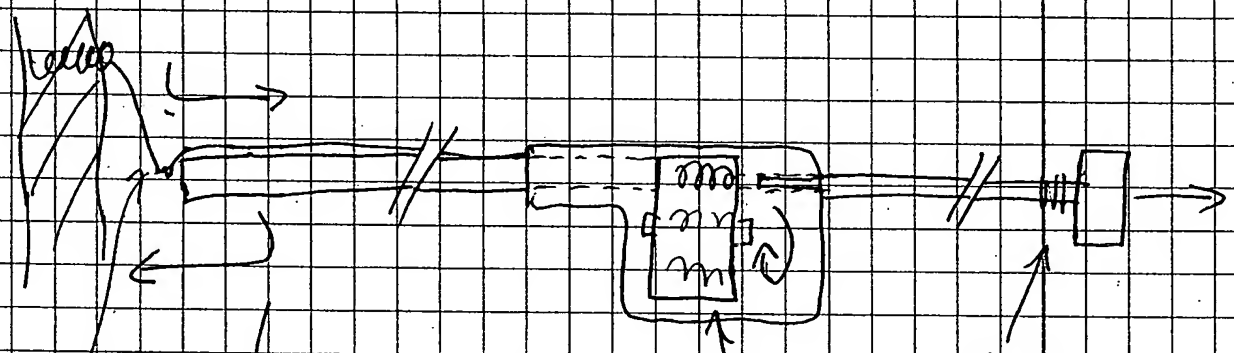
bolt screws in after threads engage causing anchor to screw into tissue.

④



bolt reversed (screwed) to retract

⑤



bolt retracted

Cable remains attached to first anchor and ready to be threaded into second successive anchors

first anchor placed, delivered tube lifted off and toward next point of anchor attachment

magazine rotated to align next anchor for delivery

Randy Lee 10/28/99

Kelly Tam 10/27/1999

Oct. 29, 1999.

Epicardial Harnessing of Explanted Porcine Heart

The harnessing patterns described on pages 86-88 were applied to the epicardial surface of a pig heart. Coil screw anchors were manually screwed into the myocardium around the left ventricle. Three bands were applied in a left hand helical pattern from the posterior to anterior surface while moving from apex to base. The anchors were connected by braided dacron string, tensions they were tightened and then tied off at the end anchors. An additional semi-circular band was applied at the base of the left ventricle around the mitral valve annulus. This was also tightened and tied off. The the following photographs illustrated the pattern.

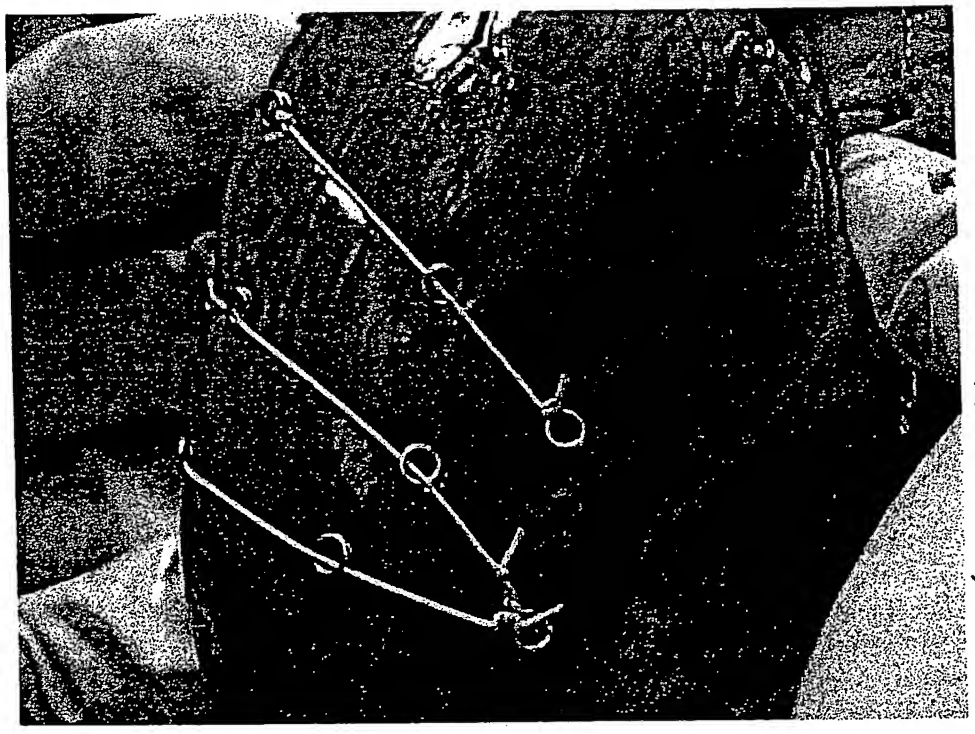
95
Oct. 29, 1999

Photo #1

Photo #2

Oct. 29, 1999

#1 10/29/1999



#2 10/29/1999

Pamela Lau 10/31/99

Kelly Tan 10/29/1999